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Perspectives in Venereology—1959

By R. R. WILLCOX, M.D. (Lond.)
(Consultant Venereologist, St. Mary's Hospital, London, W.2; Member WHO Expert Panel on Venereal Infections and Treponematoses.)

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This is the 13th of a series of annual reviews of the world's literature [this *Bulletin*, 1948, v. 23, 135–144; 1949, v. 24, 99–111; 1950, v. 25, 331–343; 1951, v. 26, 101–121; 1952, v. 27, 297–314; 1953, v. 28, 489–503; 1954, v. 29, 541–562; 1955, v. 30; 453–473; 1956, v. 31, 769–787; 1957, v. 32, 521–543; 1958, v. 33, 901–922; 1959, v. 34, 697–716.]

Introduction

The most striking developments of the year have been the deterioration in the control of venereal diseases throughout the world, recent discoveries leading to improvement in the established antibiotics, the introduction of a compound which holds considerable promise in the systemic treatment of trichomoniasis, and the introduction of screening blood tests for syphilis, capable of "while you wait" performance.

In 1958 some 27,887 cases of gonorrhoea were treated in the venereal disease clinics of England and Wales (Ministry of Health, 1959). This compared with 24,381 in 1957, 20,388 in 1956, 17,845 in 1955, and 17,536 in 1954. There has thus been an increase of no less than 59% in the 4-year period 1954–1958, and 36·7% in the last 2 years. Moreover, the 1958 figure of 17,606 cases of non-gonococcal urethritis in males was the highest on record since statistics were first published in 1951. The numbers of cases of infectious syphilis, however, continued to decline. The increase of gonorrhoea after the fall which followed World War II, commencing from around 1954, is a world-wide phenomenon, although the United Kingdom affords a most striking example. In some countries too there has been a "kick-back" in the numbers of cases of early syphilis although the total numbers are usually still relatively minute (*i.e.*, less than 5% of the immediately post-war figures). These, and other matters, were considered at the meeting of the WHO Expert Committee on Venereal Infections and Treponematoses at Geneva during the year (WHO 1959).

LAIRD and MORTON (1959), discussing the ecology of gonorrhoea, considered that the deterioration of its control had resulted from an upset of the balance of favourable and unfavourable factors. Favourable factors included effective contact tracing, improved socio-economic conditions and—in England—the implementation of the Street Offences Bill to limit street prostitution. The principal unfavourable influences were the apparently increasing occurrence of strains of gonococci less sensitive to penicillin, the presence of asymptomatic female carriers, of immigrants unlikely to become socially fully integrated, and the likelihood of expanding off-street prostitution. To which must be added the previous tendency to take less notice of venereal disease by administrators, physicians and patients alike at the time when it was mistakenly felt that these infections were virtually conquered as a public health problem.

In the antibiotic field, following the work of SHEEHAN in the U.S.A., who isolated the basic 6-amino penicillanic acid from penicillin and who synthesized phenoxymethyl

penicillin (V)—and of the British workers, DOYLE and ROLINSON, who found an economic source of this material in fermentation broth—the synthesis from 6-amino penicillanic acid of innumerable penicillin compounds is now possible. As stated by WELCH at the Seventh Annual Symposium on Antibiotics held during 1959, broad-spectrum, anti-fungal, anti-viral and even anti-tumour penicillins may be future chemical possibilities. Over 500 new penicillins have now been prepared and one—phenoxyethyl penicillin (Syncillin in the U.S.A.; Broxil in the U.K.) is now available commercially. It is claimed that serum levels may be obtained with this preparation taken by mouth which are comparable with those following penicillin-G by injection.

If the absorbability of penicillin has been improved by the addition of a CH_3 group, that of the tetracyclines has also been improved, but by the deletion of a similar group. This new dichlormethyl tetracycline (DCMT) is claimed to be absorbed 43% more slowly than tetracycline hydrochloride and a dose of only 125 mgm. 2–4 times a day is said to be necessary in most susceptible infections. If the position of penicillin and the tetracyclines is more secure, that of streptomycin is less so. Serious cases of sometimes severe and permanent nerve deafness have occurred after very small doses (1–2 gm.) of dihydrostreptomycin. In the U.S.A. it is not now permissible for manufacturers to mix dihydrostreptomycin with any antibiotic other than streptomycin sulphate, and the package must contain a warning of its possible toxicity on the eighth nerve.

Venereologists have for years required an effective drug in trichomoniasis, able to be given systemically in order that the frequent relapses encountered in the female might be prevented and so that it might also be given to the male consort simultaneously, to lessen the chances of reinfection. Hitherto drugs which have been tried have completely disappointed. First reports of a new imidazole compound (8823 RP) by DUREL *et al.* (1959) have shown encouraging results in both male and female. The drug is currently under clinical trial in venereal disease clinics in Britain.

In the diagnostic field there has been a need of a rapid blood test for syphilis, capable of being reported while the patient is still at the clinic. Such a test, requiring very small quantities of plasma or serum, has been evolved in the U.S.A. as a screening test for Mexican labourers entering California.

Antibiotics

Reactions to penicillin have been extensively reviewed for the World Health Organisation by GUTHE, IDSÖE and WILLCOX (1958) (WHO 1958), also by BROWN (1958) and by FLIPPIN (1959), who went so far as to state that the use of penicillin should be abandoned, except when it was the only antibiotic capable of the task.

4 cases of anaphylaxis to penicillin, 3 of which were fatal, were reported from the Continent of Europe (*Schweiz. med. Woch,* 1958). In one fatal case the antibiotic had been given only for catarrh. Another non-fatal case was reported by FRASER (1958), after only 800,000 units of penicillin given orally, and another, after oral penicillin G, was recorded by MARTIN (195 There is a need for a suitable test to uncover potent reactors to penicillin. Skin tests, which may give fal positive or false negative results, are an uncertain guic although JOHNSTON and CAZORT (1959) believe that th were useful in anticipating immediate dangerous anaph lactic reactions. Reactions resembling serum sickne occurred in 2% of patients given single injections benzathine penicillin by BERNSTEIN and HOUSER (195 being less common with doses below 1·2 mega units. case of peripheral gangrene and haemorrhagic purpu following administration of penicillin was reported FANG (1958).

The treatment of anaphylaxis was considered by HA (1958). A case of anaphlyaxis, in which a curare-li drug was used to permit controlled respiration, was d cribed by HEYWORTH (1958). Penicillase has been r ported by FRIEDLANDER (1959) as not useful in anaph lactic shock. Improvement followed its use in other typ of penicillin allergic reaction, but the patients might ha recovered without it. REISCH (1959) reported that pe cillinase itself might evoke serious reactions, and record 2 cases. He recommended that it should not be used the extremely young, the debilitated and the aged, w may not tolerate respiratory or cardiac embarrassme Other cases of anaphylaxis to penicillinase were report by CAPUTI (1959), HYMAN (1959) and by THOMAS (195 who also recorded a case of severe serum-sickness-li reaction.

The toxicity of penicillin to guineapigs was studied TOSHKOV *et al.* (1958): 5,0000–10,000 units killed 88 of animals, owing, it was believed, to overgrowth *Escherichia coli* and serum protein changes resulting fro the process in the bowel. This could be prevented by t addition of streptomycin, which inhibited *E. coli.* effects upon bone marrow were investigated by BOGORC SKAYA (1957). LIGHTBOWN *et al.* (1958) described method for the assay of penicillin in the blood, a WRIGHT *et al.* (1959) noted that after 1·2 mega units procaine penicillin with aluminurium monostearate t resultant penicillinaemia averaged 2·6 days, whereas t penicillin in the urine persisted for 14·5 days (ra 3–24). With 1·2 mega units of benzathine penicillin, t average duration of penicillinuria was over 3 mont They considered that the discrepancy must be related the sensitivity of the assay method and not to the abse of drug from the blood. WEISS *et al.* (1959) consider that penicillin V was no better than penicillin G penicillin-susceptible infections. If G was effective, t V could do no better. VYAS and DHOPATE (1959) no considerable deterioration in benzathine penicillin aqueous suspension kept at room temperature, altho it proved stable for one year in the refrigerator.

Chancroid

TAMPI and RAO (1958) reported that in New De approximately one quarter of all patients with vene disease had chancroid. Tetracycline (250 mgm. orall times daily for 5 days, or 200 mgm. intramuscula once daily for the same time) gave average cure ti of 4·3 days and 5 days, respectively.

Gonorrhoea

The complication of urethral stricture was considered by MARSHALL (1958). IKEJIANI (1958) reported a case of gonococcal meningitis in a Nigerian; he claimed that only 25 cases were recorded in the literature. The gonococcus proved resistant to penicillin and sulphonamides but a successful result was obtained with tetracycline.

That gonorrhoea is often asymptomatic, even in the male, was noted by LANDMAN and GELMI (1959) who reported 172 cases with little or no subjective discomfort. In the female the disease is often without signs, as noted by WILLCOX (1959) who recovered the gonococcus more often from the urethra than the cervix.

STUART and CROOKES (1959) noted that for diagnosis in the female, cultures were twice as good as smears; polymyxin B was added to the medium to discourage coliforms. A reliable fermentation medium for the gonococcus was described by THOMPSON and KNUDSEN (1958). LEJMAN (1958) noted that the gonococcus increased (sometimes 4–5 times) in size under penicillin treatment. The change was apparent within half an hour (most marked after 2–4 hours) and the affected organisms might show violet staining by Gram's stain, become irregular and deformed and then pale and shadowy as lysis occurred.

The treatment of chronic gonorrhoea was considered by PIRINGER (1959). The failure of penicillin in U.S. troops in Korea (20% failure rate after 600,000 units of procaine penicillin) was noted by EPSTEIN (1959) and increasing relapse rates after the same dose and preparation of penicillin were found in London by WILLCOX (1959a) and in Norway by GJESSING (1959). This is a continuation of the general pattern reported last year. The emergence of relative resistance of the gonococcus has been considered as likely to explain this (*Lancet* 1958).

ROCKL (1959) noted a declining mean sensitivity of the gonococcus to penicillin *in vitro* between 1956 and 1958. He considered that this might be due to selection and habituation and reserved his judgment as to whether increased resistance was occurring. With wide use, penicillin is becoming less effective, but in some places the declined powers of the sulphonamides against the gonococcus have recovered with disuse. THAYER *et al.* (1959) showed that susceptibility to sulphadiazine had returned to 97% in 1957.

Increasing failure rates have led to increased dosage of penicillin. It was considered in Iowa that 600,000 units of PAM was no longer adequate for the female and 1·8 mega units has been recommended (*J. Iowa Med. Soc.* 1958). The use of a mixed penicillin, containing procaine penicillin to give a high peak level for the less sensitive strains and a repository penicillin to give prolonged level for its epidemological advantages, was described by WILLCOX (1959b).

The declining powers of penicillin in gonorrhoea have also been observed with streptomycin. SAMPAIO and CHAVES (1958) reported 5 cases failing after 0·5 gm. of dihydrostreptomycin had been given twice daily for 10 days. 6 cases of antibiotic-resistant gonorrhoea were successfully treated with cortisone for 10–12 days, plus antibiotics, by LONGHIN *et al.* (1958) who considered that, apart from rendering encysted microbial foci permeable, cortisone enhanced the sensitivity of organisms to antibiotics.

Penicillin (Falapen) was given orally twice a day for 4 days with success by HEBERT (1959). A single dose of 750 mgm. of potassium penicillin V was given by THURMAN (1959), with 66% of cures in 18 treated, compared with 77·3% in 22 patients given 1500 mgm. over 24 hours. In Potsdam, GERTLER (1959) gave injections of rectified turpentine in olive oil to produce fever, as well as large doses of penicillin. MARMELL and PRIGOT (1959) used the oleandomycin salt of penicillin G, combined with potassium penicillin G, giving 600 mgm. of penicillin and 900 mgm. of Oleandopen—or higher doses; all of 25 patients were cured. The same authors (1959a) used tetracycline potentiated with glucosamine and found that 250 mgm. 4 times a day for 1 day gave a 94% cure rate, and 500 mgm. 3 times a day for one day cured 100%. Tetracycline alone required a dose one-third higher to achieve the same success. Similar results were obtained with the tetracycline phosphate complex (MARMELL and PRIGOT, 1959b).

Gonococcal ophthalmia

The prophylaxis of gonococcal ophthalmia was considered by RINTELIN (1959) and by AGUAYO and NAVARRO (1957).

Prophylaxis has for some years been discontinued in some parts of the world. FRANKLIN (1959) indicated that at Queen Charlotte's Maternity Hospital in London the policy was to swab the unopened eyes with sterile water at birth—prophylaxis being considered unnecessary if there was organized venereal disease control. However, MELLIN and KENT (1958) reported that, in New York, as a result of an alteration in the Sanitary Code, prophylaxis was discontinued and 3·2% of 1,974 newborn infants developed eye discharge. Gonococci were recovered by culture from 4—marked contrast to 10 in the previous 25 years. Routine prophylaxis was re-instituted.

KAIVONEN (1958) reviewed the main compounds which have been used for prophylaxis. The antibiotics were considered poor on account of bacterial resistance and allergy sensitization: the silver compounds were irritating, with but transient effect, and argyrol was not sufficiently effective. The quaternary ammonium compounds were stable in aqueous solution and reacted to storage better than silver nitrate; they could also be used to clean around the eye.

Policies on ophthalmia prophylaxis must obviously be reconsidered in the light of the increasing incidence of gonorrhoea. The Committee on Fetus and Newborn of the American Academy of Pediatrics has affirmed that gonococcal ophthalmia is still a hazard. Silver nitrate has amply demonstrated its effectiveness and the occurrence of non-specific conjunctivitis was not in itself a reason for change; the routine use of antibiotics would involve additional problems (*Sight-Saving Rev.* 1958). In Chicago, too, they have decided to retain silver nitrate (*J. Amer. Med. Ass.* 1959) and SPEIER (1957) described the use of ampoules containing 1 ml. of 1% silver nitrate, enough for one child.

Granuloma Inguinale

A biography of Charles DONOVAN (1863—1951), who described the causative organism, was presented by BAILEY and BISHOP (1959). A case was described by DIMITRESCU (1958).

Lymphogranuloma Venereum

Rectal lymphogranuloma venereum was considered by MILES (1959), who suggested that its incidence in the U.K. might increase with West Indian immigration (although, so far, such has not been the case to any striking extent).

MOLLARET (1958) concluded that benign inoculation lymphoreticulosis (cat-scratch fever) and lymphogranuloma venereum were sister diseases and true miyagawanelloses. In cat-scratch fever some patients have a positive complement-fixation reaction to antigens of the psittacosis group.

In French Guiana FLOCH and MAILLOUX (1957) had 15 positive Frei reactions in 362 apparently healthy persons. The same authors (1958) had 5·2—5·6% of positive reactions in 1,036 persons tested from Cayenne and rural areas. PEREZ-MIRAVETE and VALDEZ DE MACÍAS (1958) had positive complement-fixation reactions for lymphogranuloma venereum in 22 patients with pinta.

Sulphamethoxy-pyridazine—a long-acting sulphonamide—was used with success in 10 cases by KRISHNAMURTHI (1959). Two tablets of 0·5 gm. were given on the first day, followed by one tablet daily for 5—6 days. One patient returned with prostitis. Tetracycline phosphate (250 mgm. 4 times daily) was found effective in lymphogranuloma venereum by MARMELL and PRIGOT (1959c).

Non-Gonococcal Urethritis

The cause of most cases of non-gonococcal urethritis remains obscure. Its aetiology was considered by SIBOULET (1959) and by WILLCOX (1958), who, in 1,463 Giemsa-stained specimens, failed to find any bodies connected with the cause of the disease, although some appeared to be associated with genital inflammation. The possibility of pathogenic staphylococci being a factor in non-gonococcal urethritis was considered by MINEKICHI HIRAKIDA (1958).

Considerable work has concerned the continued investigation of pleuropneumonia-like organisms (PPLO). KLIENEBERGER-NOBEL (1959) found PPLO in 48% of 65 men with non-gonococcal urethritis but also in urethral scrapes from 30% of 49 men with untreated gonorrhoea and from 10% of 20 with Reiter's syndrome, but only in 3% of 100 healthy adults by urine examination. PPLO antibodies were found in the sera of 18·7% of 284 male and 44·5% of 416 female patients with veneral disease, but only in 2·1% and 3·7% of male and female blood donors respectively. Positive titres were thus commonly found in groups of patients in which venereal infections were rife, and from whom PPLO were cultured most commonly. In rats significant antibody titres only occurred in those infected by pathogenic organisms. Some of the above data were also presented by CARD (1959), who prepared antisera against human, animal a saprophytic PPLO in sewage. Those isolated from human genital tract were able to be distinguished se logically from the others.

GRIMBLE (1959) found PPLO by culture in 9 of patients with non-gonococcal urethritis but also in 11 90 unselected males. Positive complement-fixation te were not usually found in patients with non-gonococ urethritis who showed PPLO in culture, and he c sidered there was no conclusive proof of their pat genicity. Of 48 strains of PPLO tested by KLIENEBERG NOBEL (1959a), all were resistant to penicillin, sulpho mides, erythromycin, or oleandomycin, but were m or less sensitive to the tetracyclines, streptomyc chloramphenicol, spiramycin and neomycin.

The treatment of non-gonococcal urethritis was c sidered in a monograph by DUREL and SIBOULET (19 and by WILLCOX (1958a), who found the tetracycline a biotics best of many substances tested. KARLTORP LODIN (1959) contrasted tetracycline hydrochloride tetracycline phosphate: the latter was preferred. L (1959) had 38 cures out of 48 patients given 5—7 of spiramycin over 5—7 days.

Trichomonatous urethritis was considered by DU and ROIRON (1959). JIRA (1958) reported that the i dence of *T. vaginalis* in non-gonococcal urethritis corded in the literature varied from 1 to 73%. M were less susceptible than females, young men m susceptible than old, and the incubation period 6—10 days. He found *T. vaginalis* in 157 of 1, cases of non-gonococcal urethritis. AYYANGAR (1 found the parasite in an aberrant urethral canal in male. BURGESS (1959) examined 250 female contacts male patients with non-gonococcal urethritis, of wh 60·8% said they were symptom-free and 34·4% c plained of some discharge. Trichomoniasis was found 34·8%, while 29·8% had signs of cervicitis.

The new orally-given compound 8823 RP (1-hydr 2-ethyl-1-methyl-2-nitro-5-imidazole) was successfu used by DUREL (1959) and by DUREL *et al.* (1959) i men with trichomonatous vaginitis. No amelioration noted in 10 other cases in which no trichomonads w found. The dose given was 500—800 mgm. daily 8—10 days. This preparation holds considerable prom

Reiter's Syndrome

Reiter's syndrome was considered by CSONKA (1 and by MUTERMILCH *et al.* (1959), and 30 cases were cribed by FOURCADE and COUADAU (1958) who fo iritis common, and an additional case was reported KISTEL *et al.* (1959). A biography of Hans REITER, w nearly 400 references selected by Reiter himself, was sented by BAILEY and BISHOP (1959a). Neurological volvement in Reiter's disease was reported by Cso (1958) and by OATES and HANCOCK (1959).

OATES and YOUNG (1959) noted that sacro-iliitis o accompanied Reiter's syndrome, and was freque found in cases of relapsing iritis. CSONKA (1959a) fo 20·1% of 134 patients with Reiter's disease with ra logical signs of sacro-iliitis. Although the findings w similar to those found in ankylosing spondylitis, r

showed involvement of the spine. He considered that the two diseases were separate entities. OATES (1959), however, queried whether both conditions had a common infective agent. In both prostatitis was a common finding, although prostatitis might be found in 20—25% of routine examinations of hospital out-patients.

Ankylosing spondylitis and its association with sacro-iliitis and genital infection was considered by MASON (1959). OATES (1959a) reported that of 72 male patients with ankylosing spondylitis, 84% had chronic prostatitis: some had non-gonococcal urethritis and a significant number had previously suffered from venereal disease. GRAINGER and NICOL (1959) reported that besides Reiter's syndrome and ankylosing spondylitis, sacro-iliitis might be found in association with ulcerative colitis and destructive changes of the sacro-iliac joints might occur in patients with total paraplegia.

OATES *et al.* (1959) had urethral or prostatic cultures positive for PPLO in 9 of 54 patients with Reiter's syndrome and a positive complement-fixation reaction in 16 of 31 patients with clinically active disease. No positive cultures and only one positive complement-fixation reaction was noted in 23 males with a past history of the disease which had become inactive; on the other hand, bacteriological and serological tests reported by CSONKA (1959b) failed to implicate PPLO as an aetiological agent in Reiter's syndrome. The erythrocyte sedimentation rate and serum protein fractions were considered the best available guides to activity.

Chlorocid was successfully used in the treatment of Reiter's syndrome by VARGA (1959). In a case of keratosis blennorrhagica treated with penicillin and streptomycin by ALBERT and CRONE (1959), the condition improved but these antibiotics had little effect on the arthritis. In another case there was a striking response to steroids.

Other Conditions including Trichomoniasis

Genital lesions, venereal and non-venereal, were considered by SOBEL and CANIZARES (1959). A review of the literature of Behçet's recurrent disease was made by MAVIOGLU (1958) and vaginitis in children was considered by GROSSI and BUCHMAN (1959).

Candidiasis

Genital candidiasis was described as a new and little-known venereal disease, showing as balano-posthitis in the male and vulvo-vaginitis in the female, by RIMBAUD and RIOUX (1958, 1959). *Candida albicans* was found in 20—30% of healthy persons. The condition was aggravated by antibiotic therapy and spread by coitus. SAMPAIO and CHAVES (1958) noted an increase in vaginal thrush in prostitutes from 5% in 1955 to 32% in 1957, the increase being ascribed to the use of prophylactic penicillin. WILLCOX (1959c) used a hydroxyquinaldine compound (Gyno-sterosan) in 21 cases of vaginal thrush. In 17 patients followed there were 3 relapses, and 3 cases of vaginitis, *Trichomonas vaginalis* being recovered in 2.

Trichomoniasis

[For trichomoniasis in the male, see under non-gonococcal urethritis.]

A symposium on human trichomoniasis was held at the Nôtre Dame Hospital, Montreal, Canada, in September, 1959, and an International Study Group to promote interest in the condition has been established by the International Union against Venereal Infections and Treponematoses. (*Brit. J. Vener. Dis.* 1959). Trichomonas vaginitis was considered by FEROZE (1958) and by DE CARLE (1958). WANG and HSIA (1958) tested 1,460 females in a cotton mill in China. Trichomonads were found in the vagina of 26·9% by hanging drop and in 30·6% by culture—the total with positive findings was 31·3%. DUREL and ROIRON (1959) stated that nearly 100% of prostitutes were infected.

BUXTON *et al.* (1958), in an epidemiological study of women in mental institutions, prisons and a women's college, found a great difference in incidence. Although sexual transmission was a factor, there were other factors, as yet unidentified, but associated with socio-economic status and personal hygiene. VERHEYE and KANDA (1958) examined 912 African patients in the Belgian Congo at random; of 209 with some discharge, *T. vaginalis* was found in 107 and also in 21 of 703 others with no discharge. 37% of the wives of infected husbands were infected, and 47% of the husbands of infected wives.

HARRISON (1959) described staining methods for trichomonads and preferred Loeffler's alkaline methylene blue stain to Leishman or Giemsa—or to the hanging drop. WOLINSKA (1959) considered a trypticase culture medium as by far the most accurate. Cultures were also preferred by FILADORO and ORSI (1958) and by BURCH *et al.* (1959), who found the Papanicolau stain method the least sensitive and specific. A method of counting cell numbers in cultures of trichomonads was described by SCHOENHERR (1958) and the use of intraperitoneal injections of trichomonads into mice as a standard investigatory tool has been described (*Lab. World*, 1958).

In the past, the many local treatments used have been attained by high recurrence rates, owing to re-infection of the vagina from parasites not reached by vaginal pessaries, and also to re-infection by the consort. DE POORTER (1959) found *T. vaginalis* in the anterior urethra of 12 of 14 women with vaginal infection which would not be reached by local therapy. Even with well-tried preparations, such as Penotrane (phenylmercuric diphenylmethanedisulphonate), MURRELL and GRAY (1958) stated that 56% of their patients relapsed at least once.

Unsuccessful results with trichomycin given orally were reported by WILLCOX (1959d). Considerable interest now centres upon 8823 RP—an imidazole derivative—reported by COSAR and JOULOU (1959) as having high activity in experimental trichomonas infections in mice and possessing very low toxicity. DUREL (1959), DUREL *et al.* (1959) and Canadian workers at the First Canadian Symposium on human trichomoniasis, have presented encouraging preliminary reports of its successful action in man in doses of 500—800 mgm. orally for 8—10 days. In Durel's series *T. vaginalis* disappeared in 16 of 19 women treated,

although most (but not all) female patients had local treatment as well. The publication of the results of the clinical trials at present in progress in Great Britain are eagerly awaited.

KARNAKY (1959) noted that *T. vaginalis* cannot survive a *p*H of 1·8—2·2 and used Trimogill, which keeps the *p*H of the vagina between 2·0 and 3·0 continuously, with and without a vaginal diaphragm. He employed a battery type of *p*H machine. In patients with trichomonas vaginitis, readings were in the range of 5·0—7·6 (KARNAKY 1959a). Other local treatments, reported upon more or less favourably—with the usual reservations—included the use of bismuth and organic arsenical compounds by BORNO (1958); of emulsified Chinoform by AKIRA ISHIKI and TATSUA TODOYAMA (1958); diiodohydroxyquinaldine by PENA (1958); Gyno-sterosan by WILLCOX (1959e); hexetidine by WOLFF (1958a), and the nitrofurans by FRENCH and LANIER (1958), ENSEY (1959), KERNER and MARGALIS (1958) and by COOLIDGE *et al.* (1959), who regarded them as helpful but not as a panacea. Vasisec, which contains a chelating agent to remove the calcium from the calcium proteinate in the protozoal cell membrane, an agent to lower surface tension, and a detergent to denature the protein, was used by GIORLANDO and BRANDT (1958).

Folklore remedies were tested by WANG and HSIA (1958) in China; the vagina being swabbed with vegetable juices. Cure rates ranged from 23·4% with onion juice, 35·9% with turnip, and 17·6% with ginger; relapse rates were high.

Syphilis

General

A further annual review of the literature on syphilis (243 references) has been made by BEERMAN *et al.* (1959). Modern concepts in diagnosis and treatment have been reviewed by FLEISCHMAJER (1959) and by THOMAS (1959), and a manual on the management of syphilis has been published by the New York Department of Health. Penicillin treatment has been considered by PONCET and STRASSER (1958) and by KING (1959), who believed the antibiotic to be the drug of choice in all stages of the disease, as did DUREL (1959a), who stated that 20 mega units was sufficient in all stages.

Experimental syphilis

Rabbit syphilis was discussed in considerable pathological detail by LONGHIN *et al.* (1958a) and experimental syphilis and yaws by MATSUMOTA (1959). A fall in the vitamin B concentration of the blood during the course of experimental rabbit syphilis was noted by OHKUWA (1958), and KATSURA (1958) found that the skin lesions were more severe in rabbits with liver dysfunction than in normal animals.

SCHNEEWEIS (1958) studied the complement-fixation antigen found in supernatant material from syphilitic rabbits' testes. The immobilizing titre in mouse syphilis was studied by GASTINEL *et al.* (1958). Immobilizing substances appeared much earlier when live Nichols treponemes were used than with suspensions of the same material.

The possibility of developing a penicillin-bismu compound with antibiotic activity was considered MUSUMECI and CIACERI (1958). MUSUMECI and BONAN (1958) studied the renal function in syphilitic patie given penicillin and bismuth, and the influence of bismu on the blood and urine levels of penicillin was describ by MUSUMECI and LAZZARAO (1958).

Treponema pallidum

The action of penicillin on live treponemes was studi by VIASELEVA (1958) and the behaviour of the Reiter t ponema in media containing penicillin by GASTINEL *et* (1959). DOAK *et al.* (1959) noted that sodium chloride physiological concentration had some toxicity to *Tre pallidum*—an observation of some importance.

Early syphilis

An epidemiological study of infectious syphilis w made by SOQUEL *et al.* (1959) and the prophylaxis a diagnosis of sero-negative syphilis received attention fr GRILLMAYR (1959). As pointed out by DUREL and BOR (1958), in many cases of syphilis apparently with chancre, the chancre had been overlooked. A case rectal chancre was reported by WELLS *et al.* (195 BHARDIVAJ (1958) considered epitrochlear adenopathy a rural, mainly agricultural, Indian population; the conc tion was found equally often in syphilitic and no syphilitic subjects.

VIASELEVA (1958a), using long-acting penicillin, not that the treponemes disappeared from chancres with 4–18 hours and from secondary lesions somewhat lat ALBERTAZZI (1938) observed a febrile Herxheimer reacti in 17 cases of sero-negative primary syphilis when tre ment was begun. FELKE (1958) reviewed 286 cases early syphilis treated with penicillin; 14 of the 27 relaps or reinfections which occurred were noted in the 62 m promiscuous women, and only 13 in the remaining 2 It was concluded that the ratio of reinfection to relap was approximately 6:1. A case of penicillin-treat secondary syphilis, in which relapsing secondary tertia syphilis developed one year later, was reported by DEG *et al.* (1958). The long-term follow-up of 628 patie with early syphilis was described by CHARGIN *et al.* (195 Penicillin gave the best results.

Latent syphilis

The prognosis and treatment of late latent syphi was considered by BARNETT (1959); 80% of the cases m be seen by private practitioners (SWANSON 1959). France, 77% of syphilis is of this type and penicillin mega unit daily for 20 days) plus bismuth and mercu was preferred in its treatment by RIMBAUD (1958).

Late benign syphilis

Factors in the development of late syphilis were c sidered by CRAPS (1958) and its management by HA (1959). Although early syphilis is said to be nearly extin in France, HURIEZ *et al.* (1958) stated that there was st a considerable amount of late syphilis and described 1

cases. 25 cases of syphilomata were reported by SEBASTIANI (1958), a skin gumma in woman of 87 by ROBBINS and KIRCH (1959), and a syphilitic skin lesion of the face, resembling epithelioma, by BUREAU and BARRIERÈ (1958). Osseous syphilis was considered by KING and CATTERALL (1959); gastric syphilis by CELSO BIAGIONI (1959); and cases of pulmonary syphilis were presented by JANISCH (1959) and by SENDON (1958). Syphilitic tarsitis by TURNER (1959); and a case of syphiloma of the orbit and 2 cases of anterior segmentitis of syphilitic origin by BUREAU *et al.* (1958).

Cardiovascular syphilis

The papers of Louis GALLAVARDIN, who died in 1947, aged 82, including a number on syphilitic heart disease were reviewed by FROMENT and GALLAVARDIN (1958). Of 196 cases found during a serological survey in Brazil, most occurred 11–30 years after the primary lesion; in 23% there was additional neurological involvement (*J. Amer. Med. Ass.* 1959a).

Aneurysms of the aorta in general were considered by MIDDLETON (1959) and dissecting aneurysms by HIRST *et al.* (1958), who found the incidence of syphilitic aortitis to be low in this condition and considered that syphilitic infection might protect the aorta from dissection.

SMITH and LEONARD (1959) found linear calcification of the ascending aorta in 32 of 83 patients with syphilitic aortitis and regarded it as an almost specific sign of syphilis. The electrocardiographic findings were described by STOREY (1958) who found abnormalities in 50 of 72 patients examined, and in 33 of 34 of those with anginal pain.

WARD and READ (1959) treated 13 patients with aortic aneurysm with 20 mega units of penicillin. Improvement was noted in well-being, phonation, disappearance of dysphagia, cessation of haemoptysis and gain in weight: 9 patients were leading relatively normal lives. 3 severe Herxheimer reactions, 2 of which were fatal, following the antibiotic treatment of syphilitic aortitis, were reported by HURIEZ *et al.* (1958a).

Neurosyphilis

KIERSNICKA and WASIK (1958) found neurosyphilis in both partners in 17 of 35 married couples with late syphilis. The psychoses of syphilitic brain disease were considered by MORGAN (1958) and the electroencephalograms by MATULAY and KLUKAN (1959). Seizures in neurosyphilis were considered by FERRISS (1959) who noted this feature in 35 of 165 patients with neurosyphilis. The survival rate of patients with general paresis in hospital was described by EHRENTHEIL and MUENCH (1959).

A case of tabes dorsalis with a positive TPI reaction in the cerebrospinal fluid but a negative serum TPI was reported by FROMM and HIPPIUS (1958). The pupils in health and disease were considered by HENSON (1959) and syphilis of the optic nerves by AYYANGAR (1959). In the U.S.A., 9% of blindness is due to syphilis (HAVENER 1959). In Japan there was an increase of syphilitic eye diseases following World War II, but the incidence has now fallen to below pre-war levels (KAKISU 1958). Penicillin was considered effective in 50% of his cases, progression being halted for 7 years or more.

The criterion for the assessment of the results of treatment of neurosyphilis has been described by FURTADO (1958). The success of modern treatment has resulted in considerable economy. In Iowa it is calculated that in the period 1946–1952, some $5,780,700 had been saved in caring for patients with mental psychoses due to syphilis (*J. Iowa Med. Soc.* 1958a).

ZOLKIEWICZ-RODZIEWICZ and RODZIEWICZ (1957) reviewed the results in 146 patients with neurosyphilis treated with penicillin, arsenic and bismuth. The cerebrospinal fluid became normal in 89·2% of patients with asymptomatic neurosyphilis, 78·0% of those with meningovascular syphilis but only in 68·7% of those with tabes dorsalis. MALYKIN *et al.* (1958), in Moscow, noted that improvement in electroencephalographic findings was quicker after penicillin than after arsenical compounds.

Although penicillin may render the spinal fluid normal, the dementia of paresis may increase. Indeed, given for other causes, it may mask the later diagnosis of neurosyphilis (MACKENZIE-VAN DER NOORDAA and HAAGSMA, 1959). From the clinical as well as the pathological standpoint, KALZ and SCOTT (1958), on the long-term observation of 490 neurosyphilitics, found the results most satisfactory in meningovascular syphilis, and least satisfactory in paresis and tabes dorsalis. The lightning pains of tabes were not relieved, and for these BERTINI (1958) tried intrathecal injection of prednisone, 25 mgm. initially, followed by 50 mgm. thrice weekly for 4 weeks. Complete relief from pain, maintained during a follow-up of 3 months, was achieved in 4 of 10 patients treated, and partial improvement was noted in 3 others.

Congenital syphilis

Congenital syphilis was considered by HASSELMANN (1957) and also by WEILL (1958), who stated that Paracelsus in 1529 claimed that it was due to maternal infection. That the elimination of congenital syphilis (as a result of antenatal serum testing and the penicillin treatment of affected mothers) appears to be in sight in England was the opinion of LAIRD (1959). In Hong Kong THOMSON (1959) was successful in preventing congenital syphilis in 97·6% of 83 syphilitic women given single injections of 2·4 mega units of benzathine penicillin. DOLLKEN (1958), in considering the treatment of syphilis in pregnancy, deplored the practice of treating all pregnant women who have had syphilis with a "safety treatment" regardless of syphilitic status. Oral tetracycline (500 mgm. 4 times daily for 12 days) was used with success in 11 expectant mothers by RAJAM and SOWMINI (1959).

That the TPI antibody may sometimes be transferred passively from mother to child was indicated by BERLNGHOFF and LANGBEIN (1958). Syphilitic meningitis in an infant 5 months old, who had previously been inadequately treated with penicillin, was reported by VAISHNAVA and JADAV (1958).

The pathological changes in the teeth in congenital syphilis were described by LIPSKI and PRZYLIPIAK (1959). RAJAM and RANGIAH (1959) considered that the well treated and poorly treated infants with congenital syphilis had about equal chances of developing dental stigmata (the damage being done before treatment was

given). They quote a case in which apparently adequate treatment had been given: the conventional serum reactions were negative but reactions with treponemal antigens were positive.

Probable syphilitic gastritis in an 11-year-old female was reported by DECKER and LOUW (1959); and retrobulbar neuritis in a Hindu boy aged 9 by MISHRA (1958). 375 cases of interstitial keratitis and 144 of optic atrophy were reported by KAKISU (1958a); cortisone gave good results in interstitial keratitis with a relapse of 5%.

Serology of Syphilis

Syphilis serology was considered by PORTER (1959) and by SCHNEEWEISS (1958a), and the Annual Report of the WHO Serological Centre at Copenhagen has been presented (WHO 1958a).

The need for standardization of tests was stressed by RAJAM (1958) in an enquiry into serological procedures in India. Keeping the number of tests used to a minimum was helpful to this end. A method of preparing positive syphilitic control sera from waste material was described by JEZKOVA (1958).

That sera from patients with late syphilis may contain the rheumatic factor was indicated by PELTIER and CHRISTIAN (1959), who had 11% of 146 sera positive to late fixation tests.

Conventional (reagin) tests

Developments in complement-fixation procedures were considered by OSLER (1958) and methods of standardization by SCHNEEWEISS (1957).

Syphilitic antigens were considered by SINNECKER (1958) and the same author (1958a) noted that the use of cardiolipin antigens would increase sensitivity. The lecithins in cardiolipin were discussed by ALLEN and TONKS (1958), who described the use of alternative related compounds but none was considered to be a really satisfactory substitute. SCHMIDT (1959) tested 177 TPI-reactive and 199 TPI-negative sera with a complement-fixation test, using ordinary cardiolipin and a lecithin-free cardiolipin (Cardchol); in TPI-reactive sera the ordinary cardiolipin was superior but the lecithin-free product was better in TPI-non-reactive sera.

The results of a survey of 50,000 results of the Hecht test were reviewed by GRADWOHL (1958); an improved cardiolipin-synthetic lecithin emulsion for the Kline test was described by KLINE and SUESSENGUTH (1958); and cardiolipin antigens in the Kolmer test by MIGNE *et al.* (1959) and by SEMBRAT-NIEWIADOMSKA (1959). The use of plastic trays instead of tubes in this test was described by WIDELOCK *et al.* (1958), as was an improved method of reading it by POTTS *et al.* (1958). The Roulin complement-fixation test was described by ROULIN (1958).

In India, of a number of tests, RAJAM (1958) found the VDRL test most satisfactory, and BUBE (1958), on the basis of 7 tests made on 1,343 sera from syphilitic subjects, found it the most sensitive (97·4% of positive results). Methods of stabilizing the antigen emulsion used in this test employing benzoic acid were described by BOSSAK and DUNCAN (1958).

From many points of view there is an advantage being able to perform screening serum tests on sma quantities of blood obtained without venepuncture. KO CHUCHAROFF (1958) described the Wassermann test do with only 0·2 ml. of finger or ear blood. SCHNEEWEI and WEMMER (1957) found no differences in resu between capillary and venous blood. ANDUJAR a MAZUREK (1959) used a capillary plasma flocculation te the Plasmacrit test, with a choline-chloride modifi VDRL antigen: it proved inexpensive and useful as screening procedure.

The rapid plasma reagin test, described by SCHMI and BENTZON (1958) permits the direct use of small qua tities of untreated plasma. It proved more sensitive a no less specific than the VDRL and was considered a extremely useful screening test which would provi results before the patient left the testing centre. Th test can be done even more simply, if slightly less effic ently, with unheated serum (PORTNOY and GARSON 195 SCHNEEWEISS (1958b) showed that dried blood wou remain active for 2-3 weeks in a cold chamber and f 7 or more days at room temperatures. WOLFF (195 described a method of using desk blotting paper—a thick filter cardboard—for shipping samples of blood laboratories. Dried serum proved better than whol blood in complement-fixation tests, but all types of ser logical tests could be made from samples so prepare ITO *et al.* (1959) described simple variations in tec niques of detecting haemolysis by filter paper tests.

False-positive reactions

NICOLAO *et al.* (1958) performed serum tests for syp ilis under different artificial conditions. Increasing th concentration of total protein did not upset the compl ment-fixation reaction and produced only minor vari tions in the flocculation reaction. An increase of gamm globulin increased the positive flocculation results, wher as an increase of lipids upset the results of the compl ment-fixation but not the flocculation tests. In Afri PLAGNOL (1958) found a lowering of albumin and a increase of gamma globulin and reversal of albumi globulin ratio in seropositive cases.

False-positive serum reactions in general were consi ered by HARTL (1958), *Maryland Med. J.* (1959), and b MILLER (1958), who found that the serum electrophor tic pattern, cephalin flocculation, thymol turbidity, er throcyte sedimentation rate and complete blood count— in the order given—showed the highest incidence abnormality in biological false-positive reactions.

Human serum in various chronic diseases contain complement-fixation antibodies against antigens prepar from human tissues, especially liver and kidney. MACKA and LARKIN (1958) had only 3% of positive results in 4 normal subjects, but 22 positive results were obtained 28 cases of disseminated lupus erythematosus. Of 1 patients with viral hepatitis, 35 gave a transient weakly positive reaction, as did 4 of 43 patients wi carcinoma, 3 of whom had gastric cancer; of 79 perso with false-positive reactions, MILLER *et al.* (1959) fou 12 with systemic disease. In the tropics RANQUE a DEPIEDS (1958) found false-positive reactions in lepros viral, rickettsial and parasitic infections. PLANCH

1958) considered false-positive reactions in leprosy. The lower the albumin-globulin ratio, the greater the number of false-positive readings.

ENG (1959) showed that the titre of biological false-positive reactions might increase with time. WARING *et al.* (1958) investigated 75 persons with false-positive results and concluded that these were particularly common in persons of low socio-economic status. As indicated by TASEL (1958), some positive serum findings are due to laboratory error.

Treponemal antigens

The introduction of specific or near specific serum tests for syphilis, with treponemal antigens, has done much to define more clearly those cases in which false-positive reactions to conventional reagin tests are found. Treponemal antigens were discussed by BENAZET *et al.* (1958), BERLINGHOFF (1958), KOSTANT (1958), SIEFERT and STEINGER (1959) and by VAISMAN and HAMELIN (1958).

With conventional reagin tests the titre rises rapidly, reaching its maximum in the secondary stage of the disease, then to fall away and again to rise once more to some extent in the tertiary stage. With treponemal antigens the titre rises more slowly, to reach the maximum between the secondary and tertiary stage (SCHNEEWEISS 1958a).

Treponemal immobilization test (TPI)

As far as specificity is concerned, this, the most cumbersome and specific test, remains the standard by which all other serum tests for syphilis are measured. LAURELL and HEDERSTEDT (1959) indicated that the antibodies concerned are found in the gamma globulin zone by paper electrophoresis.

The use of the TPI test to distinguish false-positive reactions was considered by MANIKOWSKA-LESINSKA and HOFFMANN (1958); SCHERE (1958); VINIKOFF (1958) and by *J. Iowa Med. Soc.* (1959). NINARD *et al.* (1958), discussing the limitations of knowledge of syphilis serology in relation to cure, confirmed that TPI titres may persist in treated syphilus when reagin titres have diminished. HUNT (1959) emphasized that the test neither indicated the status of syphilitic infection nor the adequacy of treatment.

The TPI test was used to distinguish false-positive results in pregnancy, in a BRITISH CO-OPERATIVE CLINICAL GROUP study (1959) and by ENG (1959a), who found that about one-fifth of expectant mothers in Oslo with positive serum reactions for syphilis were false-positive reactors. In the tropics it is most useful in distinguishing false-positive results from many causes, but, as indicated, this time by RANQUE and DEPIEDS (1958), it will not differentiate between syphilis and yaws.

HARRIS *et al.* (1959) considered that the TPI test should only be done on persons with suggestive evidence of untreated syphilis and on problem sera; by this means the number of tests may be greatly reduced.

On the technical side, RANQUE and DEPIEDS (1957) tested the effects of nitrogen and carbon-dioxide on immobilization; under pressure the complement would not act and immobilization did not take place, although complement had only been suppressed and not destroyed. Streptomycin, sodium azide and thiomersalate were used as bacteriostatic agents in the TPI test by CANNEFAX (1959) and all were found to be satisfactory.

Developing from the TPI test have been the *Treponema pallidum Immune Adherence* (TPIA) test considered by ATTILI and VEZZANI (1959), and the *Treponema Disappearance (Treponemenschwundes)* (TPS) test, which has been described by FEGELER (1957). Of 150 TPI-negative sera, 148 were negative to this test and 2 doubtful. Of 214 TPI-positive sera, 198 were positive, 3 doubtful and 13 negative to the TPS test. For a positive result there had to be the disappearance of at least 80% of the treponemes recognized in the control.

Treponemal agglutination test (TPA)

The TPA test was considered by KIRALY (1959), and improved techniques by TANI *et al.* (1958). GRAM (1959) used this test on the cerebrospinal fluid and found false-positive results in less than 1%—except in meningitis. ROEMER and SCHLIPKÖTER (1958) reported on 12,000 sera tested by agglutination of the Reiter strain; they considered it a simple and satisfactory routine test and only 1% of non-specific reactions were encountered.

Treponemal pallidum complement-fixation (TPCF) test

PILLOT *et al.* (1958) found close agreement between the TPI test and complement-fixation reactions with antigens from ultrasonically disintegrated treponemes and protein extracts of same.

PORTNOY (1959) described a modification of the TPCF test, using smaller volumes of reagents (1/8 of the antigen of the regular test). That the results of the TPCF test (with the Nichols strain, ultrasonically disintegrated) almost matched those of the TPI test was the view of VAISMAN *et al.* (1958) but HEDERSTEDT (1959), although admitting that it was technically easier, found the reaction less sensitive and more easily disturbed by anti-complementary activity than the TPI test, which he felt it could not replace. In the view of BROWNE *et al.* (1959), it was not so reproducible as the TPI test.

Further adverse reports of the Treponemal Wassermann reaction in comparison with the TPI test in reproducibility and specificity, were made by SEQUEIRA (1959), LAIRD (1959a) and by DUNLOP and PRICE (1959), who presented the results in 4,105 patients tested.

Reiter protein complement-fixation (RPCF) test

D'ALESSANDRO and DARDARONI (1958) stated that syphilitic sera contained several different antibodies corresponding to different antigens in *Trep. pallidum*. The treponemal protein antigen is common to different species of treponemes, both pathogenic and non-pathogenic. CANNEFAX and GARSON (1959) demonstrated a common antigen in virulent *Trep. pallidum* and the non-virulent Reiter treponeme.

The Pallida test, with the Reiter treponeme treated by ultrasonic disintegration, was found satisfactory as a routine test by BUBE (1958). DAGUET *et al* (1958) tested

Reiter antigens of whole treponemes, protein extracts free from lipids, and purified protein extracts. All gave similar results. All kept well in the ice-box, and tests with them proved more specific but less sensitive than with cardiolipin, and somewhat less sensitive and less specific than the TPI test.

The composition of the antigen for the RPCF test was described by PILLOT and FAURE (1959). Much better results are reported on this test than on complement-fixation tests with the Nichols strain, a purified antigen of which is more difficult to prepare—as reported by SEQUIERA (1959) who used both tests.

WILKINSON and JOHNSTON (1959) found on 239 TPI-reactive sera that the RPCF test was positive in 186, the TWR in 165, the Standard Wassermann reaction (WR) in 178, and the Price preciptation reaction (PPR) in 137. On 227 TPI-negative sera, the RPCF test was negative in 225, the TWR in 153, the WR in 139 and the PPR in 167. BEKKER (1959) obtained positive results in 674 of 700 probably syphilitic sera, compared with 650 with the TPI test. Of 700 presumably non-syphilitic sera, the RPCF was positive in 16, compared with 2 with the TPI test.

The RPC test was considered of inestimable value in determining false-positive reactors by DE GROAT and MIYAO (1958), and CANNEFAX *et al.* (1959) considered it to be as reliable as the TPI and more valuable than the TPCF and VDRL in leprosy patients. The antigen is cheap, as pointed out by SCHWIMMER (1958) and costs about 1 U.S. cent per test.

FOSTER *et al.* (1959), finding the RPCF test simple, sensitive, specific and reproducible, considered it to be a good routine test, and PAVLATOU *et al.* (1958) stated that it should be used as a routine in parallel with other tests, especially when the TPI test was not made. On the other hand, VAISMAN and HAMELIN (1958) contrasted the TPI, TWR and the RPCF of 1,666 TPI-positive sera. 94·6% were positive with the TWR, 88·4% with the RPCF test, but only 61·8% with conventional tests. Of 550 TPI-negative sera, 24 were positive with the TWR, 38 with the RPCF, and 77 with the conventional tests. The TWR, with virulent organisms, was preferred.

BEKKER and ONVLEE (1959) investigated the RPCF test in rabbit syphilis. In untreated rabbits the Kolmer reaction became positive after 7–8 days, followed shortly afterwards by the RPCF and TPI reactions. In rabbits treated with penicillin within 3 weeks of the orchitis, the Kolmer reaction became negative after 4–6 weeks, the TPI after 6–10 weeks, and the RPCF after 10–20 weeks.

Intradermal (IDR) test

RANQUE and TRAMIER (1959) used an intradermal antigen, prepared from an emulsion of Nichols strain, in North Africa. It proved of no value when used alone, but was considered useful as part of a battery of tests.

* * * * *

In California the conventional serum tests are still used as a routine. If they are negative and there are no clinical signs or history suspicious of syphilis, the disease is regarded as absent. If they are positive, the serum is examined by means of the RPCF test. If result is positive the patient is treated. If it is negat the TPI test is done. If this is negative the first react is regarded as false-positive, but if the TPI is positive patient is considered as having had the disease at so time (*Science News Letter* 1959).

Treponematoses

Syphilis, a venereal disease in many parts of the wo and non-venereal in others, was reviewed by WILLC (1959f). The influence of environment on the manifes tions of syphilis was considered by LUGER (1959). M RIWEATHER (1959) reported on the endemic syphilis ca paign in Bechuanaland. Of 35,043 persons examin 9,656 had the disease. Only 2 persons with prim lesions, 287 with secondary, and 205 with tertiary lesio were found; the remainder had latent infections.

Positive complement-fixation reactions for lymp granuloma venereum were found in all of 22 patie with pinta by PEREZ-MIRAVETTE and VALDEZ DE MAC (1958). They were thought to result from "non-spe fic" reactions.

ENGELHARDT (1959) followed up the babies of pregnant women in Java in whom yaws had been di nosed. In untreated cases nearly two-thirds of infants had positive serum reactions over a 5-mo period. He concluded that yaws was congenitally tra mitted. The Kahn universal reaction in yaws was c sidered by MIKOL and SOLENTE (1958).

Yaws in S.W. Borneo was considered by VAN D HOFF (1958) and in Peru by MARROQUIN (1956), and case of bone yaws in a 5-year-old Papuan boy by V ZANEN (1958). Yaws as a factor in contracture of fingers in Africa was considered by RELVICH (19 1959a). With increasing immigration, the disease receiving more attention in Great Britain. A case early yaws in London in a 10-year-old negro boy reported by BARROW *et al.* (1959), and BLEWETT (19 considered the radiological manifestations of yaws this country. Superinoculation and reinoculation periments in yaws were undertaken by GUIMARÃES (19

The difficulties of interpretation of serum tests in ya areas, partly owing to intercurrent disease and mal trition and partly owing to the presence of endemic ponematosis, has been emphasized in Africa by DU (1958) and by GRIFFITHS *et al.* (1959). Such difficul in interpretation may occur in negroes in European co tries, *e.g.*, France (PAGES *et al.* 1959). POULSEN (1958) Guam found that the positive serum reactions may p sist for long periods, even in receding yaws, and t yaws would protect against syphilis. The danger t venereal syphilis may replace yaws, in areas cleared mass campaigns, is currently under close considerat by WHO.

Injection techniques in mass campaigns were cons ered by HACKETT and GÖCKEL (1958). In Africa the ya campaigns assisted by WHO are now in full swing. French West Africa over 2,070,000 persons have b examined, and 1,850,000 treated with penicillin. In so places the prevalence of active yaws has fallen from to 0·12%. In Ghana 2,816,900 have been examined a

,231,000 treated. In Liberia the prevalence has been educed from 19 to 4% (WHO 1959a). In Nigeria 5 nillion cases of yaws have now been treated and the 0·6% per cent. of active cases found initially have been educed to 1·3, 0·9 and 0·1%, respectively, in successive urveys (WHO 1959b). The campaign in Liberia has een reviewed in more detail by BENDEL (1959). The pidemiology of receding yaws, now increasing in impor- ance, was considered by HACKETT (1959).

Venereal Disease Control

The broad principles of venereal disease control have been outlined by GUTHE (1958) and the need for contin- ued vigilance in the present situation emphasized by CLARK (1958) and by GRYSON (1958).

The history of syphilis was considered by CAVAILLON 1959) and by HARRISON (1959a), who is a strong believer n the Columbian theory. An old belief that syphilis did ot exist but that the signs were caused by mercury poi- oning was recalled by LESKY (1958). A biography of WASSERMANN was presented by *Spectrum* (1958).

Africa

Syphilis in the Moslem population of Algeria was con- idered by MARILL and ZERBIB (1958). In Dakar, CAS- ETS (1958) found 35 of 300 pregnant women, and 32 of heir babies, sero-positive.

GRIFFITHS *et al.* (1959) used a battery of conventional erum tests on the Bantu and found a much higher dis- greement between tests than in Europe. It was con- luded that it was unwise to apply the results obtained n one population group, with those of another, who may ave been exposed to very different antigenic stimuli.

Problems related to syphilis in Africa were outlined y WILLCOX (1958b); these included the high incidence f chancroid, secondary infection of sores with non-spe- ific spirochaetes, false-positive serum reactions and posi- ive reactions due to endemic treponematoses, difficulties f contact tracing and of follow-up. It was suggested on a mass basis when no follow-up was feasible, that all patients with genital sores should be given 2·4 mega units of PAM, without tests, the sulphonamides being given when the sores failed to heal.

Asia

The venereal disease control programme in Manila was outlined by IBARRA (1959). In Taiwan 5% of preg- nant women and 3·4% of blood donors were sero-posi- tive (FRÖHLICH 1958). In Japan, from a one-day survey made in 1955, it was estimated that no less than 720,000 cases of venereal disease occurred annually, and 8·8 million man days were lost during that year (TANAMI and YAMAMOTO 1958). TAMPI and RAO (1958a) con- sidered the occupational status of patients with venereal disease in India.

Europe

The venereal disease control programme in France was considered in historical perspective by PETIT-MAIRE and DARTIGUES (1957) and that in Italy by DEL VECCHIO (1959).

GOODMAN (1958) considered that Finland (population 4,100,000) appeared to have no problem of venereal disease, prostitution or of male homosexuality. Syphilis morbidity was reported as rising again in France (REBOUL *et al.* 1958) and whereas gonorrhoea is increasing markedly in England and Wales, early syphilis, which showed a minute rise in 1956, has again fallen below the 1955 level (*Brit. J. Vener. Dis.*, 1959a).

U.S.A.

Although between 1946 and 1957, with the decline in venereal disease, there had been an estimated saving in expenditure in New York City alone of 2½ million dollars. ROSENTHAL (1959) reports that the numbers of cases of both gonorrhoea and early syphilis are now rising again. In Massachusetts there was a 9% rise in syphilis rates, and a 15% rise in infectious syphilis in 1958 (*New England J. Med.* 1958); a deterioration in national sex habits was suggested as a cause of this, considerable blame being attached to parents. ANDERSON (1958), however, considered that the recorded increase in syphilis might be due to better reporting. Nevertheless, FIUMARA *et al.* (1959) estimated that there were probably 1,250,000 cases of syphilis in the U.S.A. requiring treatment, and approximately one million cases of gonorrhoea occurred each year.

The venereal disease programme in New Mexico (including the Navajo Indians) was outlined by DJANG *et al.* (1959).

Case-finding

SOQUEL *et al.* (1958) studied a chain of syphilitic treatment involving 326 persons, 27 of whom were infected. The contacts were treated prophylactically even in the absence of signs; this measure was considered essential. FIUMARA *et al.* (1959a) studied an outbreak of gonorrhoea started by a single individual and involving 26 persons.

DIJON (1958) quoted a case in France where a lady obtained an indemnity of 20,000 francs when, by mistaken identity, she was required to attend for medical examination as a contact.

Routine serum testing continues to be a valuable method of contact-tracing, but its usefulness declines as syphilis becomes less common. In Maine, U.S.A., in 1956, it was estimated by LABRACK (1958) that 78-80% of pregnant women had the test as prescribed by law. In Georgia, BROWN and SUNKES (1959) reported that of 25,586 pre-marital tests, 3·1% showed reactivity. With the decline in syphilis a shift is occurring in positivity rates to routine tests. VOR DEM ESCHE (1959) reported that in blood donors, only 2 in 10,000 in the 18—30 age-group were sero-positive, compared with 20 per 10,000 in the 30—60 age-group.

Much venereal disease is treated by private practitioners and the need for experienced investigators to aid the physician in contact investigation was stressed by TEAGUE (1958) and methods of obtaining the co-operation of physicians in reporting cases were considered by MAGALLON (1959). At the same time, THOMAS (1958) felt

that improved training was required for general practitioners since the treatment of syphilis was now largely in their hands.

In Great Britain a study made in 1956 by the British Co-operative Clinical Group and British Medical Association showed that in 4 areas, if the cases of venereal disease treated by practitioners had been reported, there would have been a rise of one-quarter in the syphilis figures and of one-seventh in gonorrhoea and non-gonococcal urethritis (BRIT. CO-OP. CLIN. GROUP, 1959a).

Problem groups

Problem groups particularly exposed to the risk of venereal infection include teenagers, migrants, prostitutes and homosexuals.

In Iowa 51·6% of all gonococcal infections occurred in young people 15—24 years of age, but only 17·7% of syphilis. It was considered likely that in reality syphilis had the same distribution but there was a failure to diagnose the disease early enough (*J. Iowa Med. Soc.* 1958b).

The World Directory of Venereal Disease Treatment Centres at Ports (WHO 1959c), published by WHO, succeeded the 1951 directory. It contains particulars of the Brussels Agreement. The Mexico border programme, which screens migrant farm workers entering the U.S.A. for venereal disease, has been outlined (*Pub. Health Rep.* 1958), and described by ROBINSON (1958). The recruitment of Mexican labour started as a war measure and continues on a large scale. Each labourer under contract is sprayed with an insecticide, vaccinated, has a chest X-ray and is examined for venereal disease. In a period of just over 2 months some 47,579 migrants were examined at El Centro, California. The rapid plasma reagin test was used, and MATTHIAS (1958) reported that 8·2% of sera were reactive.

Problems of prostitution in relation to venereal disease were considered in a United Nations publication devoted to prostitution by WILLCOX (1958c), by SAMPAIO and CHAVES (1958) and by GRYSON (1958). The venereal disease morbidity in French prostitutes in Paris was reported by LAPORTE *et al.* (1958). WONG and WANG (1958), in Taiwan, found a sero-positivity rate of 10·6% in prostitutes, 17·6% in femal entertainers and 21·6% in hotel maids. Gonorrhoea was found in 32·0% of those aged 16—20. In 1956 in Japan the number of prostitutes was estimated at 150,000, and 72% of venereal disease occurred in prostitutes or their male partners (OHNO *et al.* 1958). A new law passed in 1958 made collective prostitution illegal. In Greece a law of 1955 closed the brothels and abolished collective prostitution, but all prostitutes still report to the health authority once a week (WHO 1958b). In Italy DEL VECCHIO (1959) reported that 69,000 prostitutes were examined in 1955, and 56,000 in 1956. In both years over 30% had some disease. Infectious syphilis was found more frequently in those outside the licensed houses.

In the Philippines IBARRA (1959) reported that, of males with venereal disease, 50% were infected by prostitutes, 36% by waitresses, and 13% by hostesses. In Malaya HOLMES (1959) estimated that prostitutes were responsible for nearly all gonococcal infections in male.

Homosexuality and venereal disease was considered GOODMAN (1958a) and by LARSEN (1959), who stated homosexual males appeared to be more promiscuo than their heterosexual counterparts.

Prophylaxis

OHNO *et al.* (1958) stated that foaming vaginal pe cillin tablets were able to produce a good vaginal co centration of penicillin without entering the blood strea and were used as a prophylactic against venereal dise by prostitutes in Japan.

FOOTNOTES

The majority of the papers listed, or abstracts of the were published during 1958 in this *Bulletin*, the *Tropi Diseases Bulletin, Abstracts of World Medicine* or *British Journal of Venereal Diseases.* The author is a indebted to the Public Health Service of the U.S. Depa ment of Health Education and Welfare, and to World Health Organization, for additional informati provided, especially for the *Abstracts of Current Lite ture* published by the former. Owing to the printi strike during 1959, some articles in British journ appeared too late for inclusion during this year's revie

Where papers are by two authors, the name of ea author is listed in the text: where three or more auth have collaborated, the name of the first with the te *et al.* is used, but the names of all authors are given the list of references.

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Public Health

The order in this section is:—**General; Vital Statistics; Epidemiology; Maternal and Child Health; Health of Students, Nurses and Hospital Staffs; Health of Old Persons and the Chronically Ill; Chronic Cardio-Respiratory Diseases; Chronic Rheumatism; Cancer; Miscellaneous Diseases; Dental Health; Mental Health.**

GENERAL

CHALKE, H. D. **Public Opinion on Health Education.** *Med. Officer.* 1960, Apr. 22, v. 103, No. 17, 239–41.

This article by the MOH of Camberwell Metropolitan Borough is an attempt to assess the relative values of different media used in health education.

A form containing 5 questions was made available for distribution at the Town Hall, public libraries, clubs, welfare centres, a departmental store and a secondary modern school. The 604 completed forms are analysed by age, sex and occupation. (The article does not give the numbers in each group.) The number of forms available was 3,700.

The questions were (1) Please give your own view of the order of importance of the following as a means of health education: (a) magazines such as *Family Doctor*, (b) newspaper articles, (c) pamphlets, (d) posters, (e) films, (f) exhibitions, (g) radio programmes, (h) television programmes, (i) visits to maternity and child welfare centres, (j) talks at clubs, (k) talks at school. (2) Have you been visited by a health visitor or other social worker and did you find the advice of benefit? (3) What recent item of health propaganda impressed you most? (4) Is commercial advertising more effective than health propaganda? (5) Should more money be spent on advertising health: if so, have you any suggestions on how to spend it?

The answers to question (1) showed that television was voted first by all groups except (a) those from the secondary modern school whose first choice was films and (b) men over 60 who put newspaper articles first. In most groups pamphlets were at the bottom of the list followed by talks at clubs and exhibitions.

Question (2) was not put to school children but of the adults 91 had been visited and 73 had found the advice helpful.

The subjects which had made the greatest impact recently were poliomyelitis and smoking and cancer.

A majority, 61%, considered that commercial advertising was more effective than health propaganda.

In answering question (5) 450 thought that more should be spent on health publicity and 113 of them that it should be used for television programmes.

In the 26–35 age group it was felt that there should be more health films shown in schools.

The author points out that much less interest was

shown in the enquiry by the unskilled worker than by the skilled and professional and stresses that his results apply only to a small section of his borough. The media of health education used in any locality should have regard to the type of inhabitant as what attracts one type may repel others.

[This is one of the few attempts to find out how the public react to different media of health education and should be repeated elsewhere. A further stage would be to discover how people of different levels of education can be motivated to overcome apathy about such thin as vaccination and to cut out undesirable habits.]

Allen Daley

GILBERT, Jules. **[Health Education Theory a Practice.]**

This book was reviewed on p. 525.

VITAL STATISTICS

ALLAN, T. M. **British Stillbirths and First Week Deaths, 1950–57.** *Brit. J. Preventive & Social Med.* 1960, Jan., v. 14, No. 1, 35–8.

The sex ratio of stillbirths in England and Wales fell from 1928, the year when stillbirths were first registered, to 1938 and then remained fairly constant around 1·17 to 1952 when the rate declined falling to 1·08 in 1957. In Scotland from 1939, the first year of registration, the rate declined fairly steadily from 1·23 to 1·08 in 1946 and then rose to 1·16 and then fell somewhat irregularly to 1·01 in 1957. This sex ratio was lower than that of the live births. The fall in the sex ratio of stillbirths in England and Wales was due to a rise in the female stillbirth rate which was higher in each of the 4 years 1954–57 than in any of the 4 preceding years. In Scotland the female rate remained practically stationary 24·5 per 1,000 female births in 1953 and 24·2 in 1957. The cause of the sex differential in England and Wales cannot be found because the causes of stillbirths are not registered. A comparison has been made with the Netherlands where the female stillbirth rate was 17·6 per 1,000 female births in 1950–53 and 16·3 in 1954–57; in England and Wales the corresponding figures were 21·3 and 22·3. The mortality sex ratio rises during the first days of life; during 1954–57 the ratio was 1·09 for stillbirths and 1·78 on the fourth day in England and Wales and in Scotland 1·05 and 1·79, respectively. *W. J. Martin*

BENNETT, F. J. **Mortality in a Rural Zulu Com munity.** *Brit. J. Preventive & Social Med.* 19€ Jan., v. 14, No. 1, 1–8. [24 refs.]

The rural district was Polela in south-west Natal wi a population of 10,600 persons. The district is ove crowded and not self supporting, about three-quarte of the males between ages 25–40 are away most of t time working in towns. The area has good preventi and curative medical services. The infant mortality f from 202 per 1,000 live births in 1945–46 to 86 in 1955–5 deaths of children under 1 year comprised about or quarter of the total deaths. The death rate declined fro 24 per 1,000 of the population to 12 during the 10 yea The cause of death of about ¼ of the total deaths w unknown; the most common of the diagnoses were tube culosis, dysentery, violence and hypertensive heart failu The authors have outlined the social and economic co ditions of the people and the effects on mortality. T decline in mortality can be attributed to the improv ments introduced by the health services but much of t mortality is not amenable to medical treatment a poverty appears to be the root cause of kwashiork among children. Kwashiorkor has three peaks during t year due to environmental factors.

[See also this *Bulletin*, 1957, v. 32, 6.] *W. J. Martin*

MATERNAL AND CHILD HEALTH

BIENER, K. Schulhygiene in Ägypten. **[School Hygiene in Egypt]** *Ztschr. f.d.g. Hyg. u. ihre Grenzgebiete.* 1960, Mar., v. 6, No. 3, 157–67.

In the United Arab Republic an extensive system for promoting the health and welfare of youth is being developed. Among the 24 millions of population in Egypt, 2 million children of the 6–12 age-group attend primary school, 450,000 of 12–15 age-group attend intermediate school and there are secondary schools for 300,000 children 15–18 years of age. There are also special schools. The organization and development of schools is supervised by the School Health Department which is also concerned with the 3 Egyptian universities.

There is in this paper a wealth of information on man subjects of importance. A determined effort is bein made to lessen illiteracy which among adults is abo 30%. Particular attention is now given to the educatio and welfare of women. In Cairo there are 18 centres f maternity and child welfare. Vaccination against sma pox and immunization against whooping coug diphtheria and tetanus is obligatory. The campaig against tuberculosis—there are 250,000 "reported case of the disease in the whole country—is being develope and BCG vaccination is obligatory in Cairo in the fir 12 months of life.

Tables set out the incidence of diseases in the childre in the 3 types of school. For example in primary scho

hildren trachoma is present in 38%, schistosomiasis in % (14% in intermediate schools) and helminthiasis in 4%.

Some particulars are also given of methods of instruc-on in the schools, the care provided by school nurses nd social workers, the number of medical inspections arried out and the methods of examination adopted by ie school doctors, who number more than 1,000.

There is hospital accommodation reserved for sick schoolchildren, and also special clinics for a variety of conditions including dental defect, salmonella infections and ascertainment of schistosomiasis.

Mention is also made of school canteens, and of the emphasis placed on health education.

M. E. Delafield

HEALTH OF OLD PERSONS AND THE CHRONICALLY ILL

HELDON, J. H. **Problems of an Ageing Population.** *Brit. Med. J.* 1960, Apr. 23, 1223–6.

In view of the author's high reputation and his ioneering work in Wolverhampton, any article written y him on the care of the elderly is read and carefully igested by all interested in geriatrics. In this article he rst outlines the now well recognized changes in the age tructures of populations and the social revolution that s arising from them. His main theme however is to ivide the problems of old age into those of the main-enance of independence in the early period of old age, which he suggests might be arbitrarily taken as up to he age of 75, and those of custodial care in the later eriod. For the former he refers to the great value of earing aids, spectacles, meals on wheels, chiropody, lubs, suitable housing and particularly good neighbours. The reviewer was disappointed that he only just men-ioned employment.]

In relation to custodial care, he emphasizes the impor-ance of a true partnership between the geriatric physician nd the family, in which the latter plays the dominant ole. He describes in general terms how this may be stablished, and urges early discussion between the con-ultant and the family of problems that are likely to rise, and the promise of re-admission to hospital when difficulties arise.

C. O. S. Blyth Brooke

ROTH, M. **Problems of an Ageing Population.** *Brit. Med. J.* 1960, Apr. 23, 1226–30, 1 fig. [20 refs.]

The increased proportion of mental illness resulting rom the increased proportion of aged in the population vith a consequent shift of the incidence from schizo-phrenic and neurotic forms to manic-depressive types, is irst brought out. It is considered that there are some 50,000 cases of senile psychosis alone in Great Britain, nd that in a high proportion of these cases apathy, depression, fear and hopelessness, play a part.

Nevertheless 95% of the elderly are probably integrated n the community though 10–15% only barely so, and if hese marginal cases should break down they might well overwhelm the services.

Although mental illness may be partly hereditary it has been shown in South Africa that there is an increased hazard among the poor and undernourished, and there is a growing appreciation in psychology as in medicine that much that formerly passed for senescence is a consequence of disease, whose signs, as is recognized in pneumonia, may be absent.

Mental difficulties may be the culmination of the effects of adverse influences over many years and should be anticipated. The main sources of vitality in old ages are the nutritional, intellectual and emotional acquisitions in earlier life, and there should be ample outlets for creative gifts before 40.

Finally, great stress is laid on the need for early diagnosis of mental stress in order that treatment may be initiated immediately.

C. O. S. Blyth Brooke

GIBSON, R. **The Elderly Dane.** *Brit. Med. J.* 1960, Apr. 23, 1231–5.

This is a general account of the services for the elderly provided in Denmark as seen by a general practitioner who spent 10 days in the country in their study.

It would seem that in their operation they resemble fairly closely those available in the United Kingdom, but enjoy greater co-ordination both in policy and performance owing to the existence of a Ministry of Social Affairs.

A description is included of the Old People's Town in Copenhagen which covers 26 acres, and has accommodation in three sections for 500 wholly dependent persons in hospital, 300 semi-dependent and 1,600 or more who have not reached the stage of dependency. Although officially described as a town, it was, in effect, found to be little more than a large institution.

C. O. S. Blyth Brooke

RICHARDSON, I. M., KLOPPER, K. M. & LYNCH, G. W. **Special Housing for Older People. A Study of Eighty Households in Aberdeen.** *Med. Officer.* 1960, Apr. 14 & 22, v. 103, Nos. 16 & 17, 219–24; 235–8.

The housing policy in Scotland has been influenced and guided by the 1952 Report of the Scottish Housing Advisory Committee and the investigation described in the articles was undertaken to evaluate the results of this policy in regard to the elderly. Visits were paid to 80 representative houses built for elderly persons in the last

10 years in Aberdeen; enquiries were directed to discover the extent to which the location and the character of the houses served the purpose of providing for the health and happiness of those living in them.

The answers given are analysed in some detail and then a short discussion ensues on the success achieved in regard to each of 13 specific recommendations of the 1952 Report. The articles are worthy of study by those interested but it is impossible to summarize the data.

C. O. S. Blyth Brook

CHRONIC CARDIO-RESPIRATORY DISEASES

DOWLING, H. F., MELLODY, Margaret, LEPPER, M. H. & JACKSON, G. G. **Bacteriologic Studies of the Sputum in Patients with Chronic Bronchitis and Bronchiectasis. Results of Continuous Therapy with Tetracycline, Penicillin, or an Oleandomycin-Penicillin Mixture.** *Amer. Rev. Respiratory Dis.* 1960, Mar., v. 81, No. 3, 329–39, 1 fig. [17 refs.]

This paper describes monthly bacteriological studies of the sputa of 89 patients with bronchiectasis or chronic bronchitis. The patients were treated for periods of 3–31 months with 2 gm. tetracycline, 1 gm. potassium penicillin G, 2 gm. oleandomycin-penicillin mixture or a sucrose placebo daily, there being 4 treatment groups into which patients were placed in rotation as they entered the study. The drugs were dispensed in identical capsules, individual doses being taken 4 times daily. Patients were occasionally placed out of strict rotation by a disinterested member of staff to balance the groups with regard to age, sex, and complications such as hypogammaglobulinaemia. Various culture media were employed, purulent flecks from washed and unwashed samples of sputum being used to inoculate the plates. Pancreatin digestion of the unwashed sputum samples was discontinued early in the study.

In an earlier communication [this *Bulletin*, 1959, v. 34, 1080] it was reported that lower respiratory illnesses were more common in patients from whose sputa *Haemophilus influenzae, Staphylococcus aureus* or pneumococcus was cultured, and less common in patients receiving tetracycline or oleandomycin-penicillin therapy.

In the present study the authors found that tetracycline or oleandomycin-penicillin therapy brought about a significant diminution in the frequency with which *H. influenzae, Staph. aureus* or pneumococcus could be isolated from sputum as compared with placebo therapy.

They found no tendency towards development of drug resistance in the treated groups and no increase in the frequency with which yeasts were isolated in the treated cases, as compared with placebo group. Tetracycline-resistant strains of *Staph. aureus*, however, were found more frequently in patients treated with that antibiotic. This the authors ascribe to the efficiency of tetracycline therapy in preventing the implantation of drug-sensitive strains.

They found no significant increase in the number of other pathogens during therapy except that *Proteus* was isolated more frequently from patients of the oleandomycin-penicillin group and *Pseudomonas* from those of the tetracycline group. In none of the patients were the organisms found consistently after the inception of therapy. The authors conclude that the tetracycline regimen was the best therapy used.

Frank Russell

CANCER

WATLER, D. C., BRAS, G. & MCDONALD, H. G. **The Incidence of Malignant Neoplasms in Jamaica.** *West Indian Med. J.* 1959, Dec., v. 8, No. 4, 249–61, 3 figs. [24 refs.]

A cancer registry was set up in Jamaica in 1957 with the intention of registering all the cases of cancer diagnosed in the metropolitan area of Kingston and St. Andrew. Medical facilities are poorly developed in country areas and it is impossible to estimate the incidence of cancer throughout the island. The present data relate to cases diagnosed for the first time in 1958 among persons permanently resident in Kingston and St. Andrew (population 367,000) and it is believed that only a few cases in this population escaped registration. The data are compared with those recorded by the Danish Cancer Registry for all Denmark over the period 1942–44. The annual morbidity rates for all cancer are closely similar for all age-groups and both sexes in both countries, but the distribution by site is notably different. In Jamaica, the numbers of cases of cancer of the upper alimentary and respiratory tract and of the oesophagus are higher in both sexes than would have been expected on the basis of the Danish morbidity rates, and the numbers of cases of cancer of the penis in men and of cancer of the cervix uteri in women are also higher. In contrast, cancers of the stomach and of the small intestine, colon and rectum are only half as common. Cancers of the lung and of the liver are somewhat more common than in Denmark but the differences are small. Cancer of the lymphatic system (including leukaemia) has the same frequency as in Denmark.

Comparison of the data with those recored for various communities in Africa show similarities in the incidence of cancer of the gastrointestinal tract and of cancer of the cervix uteri. The incidence of cancer of the oesophagus is similar to that recorded among South African Bantu but it is much greater than that recorded elsewhere. The frequency of cancer of the liver is substantially less than that reported for many parts of Africa.

Richard Doll

WORLD HEALTH ORGANIZATION. TECHNICAL REPORT SER. NO. 192. **Epidemiology of Cancer of the Lung. Report of a Study Group, Geneva, 16–20 November 1959.** 13 pp. 1960. Geneva: Palais des Nations. [Sales agent for U.K., H.M. Stationery Office.] [1s. 9d.; $0.30; Sw.fr. 1.–.]

The Study Group reviewed the present evidence on aetiological factors. It unanimously agreed that the sum total of the evidence was most reasonably interpreted as indicating cigarette smoking as a major causative factor in the increasing incidence of carcinoma of the lung. While some of the criticisms of that belief suggested avenues for further research, none, it concluded, cast any serious doubt on the main conclusion. Air pollution could also be a factor of importance but in many countries its role appeared to be smaller than that of cigarette smoking. The contribution of known or suspected specific occupational causes is quite small but more precise definition of the conditions under which they produce lung cancer might lead to important knowledge of the mechanism of carcinogenesis in man. There is insufficient evidence of the importance, if any, of ionizing radiation from non-industrial sources, of previous respiratory infections and of heredity. With regard to the last it is noted that the fact that identical twins show a greater similarity in their response to exposure to environmental agents (such as alcohol and tobacco) than do fraternal twins does not provide evidence that the apparent effects of such agents are also genetically determined.

The Study Group strongly recommended more large-scale epidemiological investigations to throw light on the causes of the wide geographical variations in mortality that are known to exist. As one example, the death rate for cancer of the lung is about 5 times as great in Finland as in Norway for males, but less than twice as great for females. Epidemiological studies of possible factors in this situation would be very worthwhile. Other studies of importance would relate to certain large groups of persons not exposed to one particular aetiological agent, but exposed to another, *e.g.*, the Seventh Day Adventists in the U.S.A., who do not smoke but are exposed to air pollution [this *Bulletin*, 1960, v. 35, 333]; and to groups of persons specially exposed to particular factors, *e.g.*, industrial workers exposed to specific fumes, etc. One method of conducting a genetic study would be to identify the first member of a pair of twins who develops cancer of the lung, to obtain information on the exposure of both twins to various suspected exogenous factors, and then to keep the other twin under observation. While epidemiological studies may identify general factors affecting incidence, the identification of the specific underlying agent responsible may well need laboratory and experimental work. Such work should be encouraged.

The Study Group's main concern was to consider the ways and means of further research but in conclusion it "wished to call attention to the fact that existing knowledge of the etiology of lung cancer is already sufficiently well established to justify prophylactic action aimed at reducing exposure to known etiological factors."

A. Bradford Hill

HAMMOND, E. C. & WYNDER, E. L. **Cigarette Smoking and Lung Cancer in Canada.** *Canadian Med. Ass. J.* 1960, Feb. 13, v. 82, No. 7, 372–7, 3 figs. [20 refs.]

The authors are engaged upon studies of cigarette butt lengths in different countries and present here their findings for Canada. In January and February, 1959, 6,428 discarded butts were collected in Montreal, Toronto, Vancouver and Hamilton from many different locations —private homes, restaurants, offices, factories, streets, etc. and in neighbourhoods classed as upper-class, middle-class and lower-class. In total the mean length of butt was 27·9 mm. compared with 30·9 mm. in the U.S.A.

Length of butt (mm.)	U.S.A. %	Canada %	Netherlands %	England and Wales %
< 10	0·8	0·1	1·8	1·2
10–14		1·7 (1·8)	13·8 (15·6)	17·5 (18·7)
15–19	7·9	12·9	32·4	46·7
20–24	19·7	22·9	28·7	25·4
25–29	19·9	24·0	13·0	6·9
30–34	20·9	18·3	5·3	1·4
35–39	12·8 (51·7)	9·7 (38·4)	2·9 (10·3)	0·6 (2·3)
40+	18·0	10·4	2·1	0·3
Total butts measured	4283 (100%)	6428 (100%)	890 (100%)	772 (100%)
Mean length (mm.)	30·9	27·9	20·8	18·7

[this *Bulletin*, 1959, v. 34, 46], 18·7 mm. in England and Wales [*ibid.*, 1959, v. 34, 444] and 20·8 in the Netherlands [*ibid.*, 1959, v. 34, 541]. Only 1·8% of the butts were less than 15 mm. in length compared with 18·7% in England and Wales, while at the other end of the scale nearly 40% were 30 mm. or more in length compared with only 2·3% in England and Wales [see Table on p. 745].

The mean length decreased with the social class grading of the neighbourhood (from 31·4 to 27·8 to 25·5 mm.). Butts with lipstick marks were presumed to have been smoked by women and had an average length of 28·5 mm. compared with 27·8 for the remainder. There was no significant difference in length between filter tip cigarettes (28·3 mm.) and non-filter tip cigarettes (27·3 mm.).

Substantial differences in the length of cigarette smoked, of the kind reported here, may well explain, or contribute to, observed international and social class differences in mortality from cancer of the lung.

A. Bradford Hill

MODY, J. K. & RANADIVE, K. J. **Biological Study of Tobacco in relation to Oral Cancer.** *Indian J. Med. Sci.* 1959, Dec., v. 13, No. 12, 1023–37, 12 figs. on 3 pls. [20 refs.]

Oral cancer contributes a large proportion of the cancers found in India and there is evidence that this type of cancer is related to the habit of keeping a quid of tobacco rubbed together with slaked lime in the lower gingivo-labial groove [this *Bulletin*, 1955, v. 30, 686]. A study was, therefore, undertaken to see whether cancer could be produced in experimental animals by extracts of sun-cured tobacco.

Two strains of albino mice (A and Swiss) were used. In some animals the skin was painted, in others the buccal mucosa. Untreated animals and animals treated with benzene or chloroform solvents or with 3:4-benzpyrene in benzene were observed as controls. Others were treated with alkaloid-free extracts—water, benzene, petroleum ether or alcohol—of the tobacco leaf. After the first month of painting, shell lime was added to the extracts used for painting the buccal mucosa. The experiments were started when the mice were aged 2—3 months and were continued until the animals died or appeared emaciated, when they were killed; in the majority of instances they were killed between the ages of 12—18 months. Sections of the skin or of the buccal mucosa were examined histologically and the internal organs were examined at autopsy. In a total of 448 mice there were 3 cancers of the skin (1 spindle cell sarcoma in a mouse painted with benzene extract and 2 carcinomas in mice painted with 3:4 benzpyrene) and there was 1 cancer of the buccal mucosa (in a mouse painted with chloroform solvent). Somewhat more hyperplasia of the skin was observed in the mice painted with extracts than in those painted with solvents, and a slight thickening of the buccal mucosa was occasionally seen in both the solvent and extract groups. No precancerous changes were observed. Tumours of the internal organs were seen in all groups without any specific concentration.

A screening test for carcinogens (early disappearan of the sebaceous glands) was negative with seve extracts and pure gamma-sitosterol (a compound isola from tobacco). Alkaloid-containing extracts rapi caused death, but it may be significant that they a produced massive hyperplasia of the skin with disappe ance of the sebaceous glands. Single subcutaneous inj tions produced a high mortality; many of the animals t survived showed tumours of the internal organs and c showed a local fibrosarcoma of the skin which was tra plantable. *Richard Doll*

NAKANISHI, Y. H., MIZUTANI, M. & POMERAT, C. I **Smoke Condensates on Lung Cells in Tissue Cu ture with special reference to Chromosom Changes.** *Texas Reports on Biol. & Med.* 19 v. 17, No. 4, 542–90, 96 figs. on 18 pls. & 11 te figs. [36 refs.]

Studies on cell cultures from lungs of kittens and human foetus showed that treatment with tobacco smo condensate produced morphological changes in dilutio down to 1 in 6,400. A 1 in 10,000 dilution was, therefo chosen to see if any effect could be observed on chrom some number or morphology. Smoke condensate w added to the nutrient fluid employed for the maintenan of human foetal lung cultures and all samples were tak for chromosome examination at intervals up to 28 da after 28 days the treatment was stopped and the cultu were maintained for a further 2 months. Subcultu were then made every 4 to 7 days for over a year.

On the 8th day the control subcultures showed t majority of cells to have chromosome numbers of 46 48, whereas the treated cultures showed peak numbers 43 to 46. Subsequent examinations up to the 28th d (treated) and 30th (control) showed greater diversity number. No gross morphological differences betwe the cells in the two series were noted. Both series subcultures resulted in the progressive dominance epithelial-like cells. For some time there was a wi scatter of the chromosome distribution, but eventua the control cells came to show a peak of 77 chromosom and the treated cultures a peak at 76 chromosomes. It concluded that pretreatment with smoke condensate d not play any important part in the establishment of t cell strain.

Cells from the control strain were treated on su cultures with 0·01 mgm. per ml. of one of two smo condensate fractions and compared with untreated a acetone-treated controls. Both control cultures continu to show modal chromosome numbers of 77, but t treated cultures gave scattered distributions until eve tually the modal number settled at 76. In the peri when the change of chromosome numbers occurre dicentric chromosomes appeared in each of the treat series. It is presumed that these abnormal chromosom resulted from fusion. Similar changes were observed cultures of the control strain treated with either benzp rene, or benzpyrene and smoke condensate. A simil type of change was also found in cultures of hum amnion irradiated with 1000 r. *Richard Doll*

DENTAL HEALTH

CLARKE, J. H. C. & MANN, J. E. **Natural Fluoridation and Mottling of Teeth in Lincolnshire.** *Brit. Dental J.* 1960, Mar. 1, v. 108, No. 5, 181–7, 5 figs. [12 refs.]

In this paper there is an interesting description of the geology of Lincolnshire in relation to the underground water supplies and the differences in the concentration of fluoride in various areas. From these observations it is concluded that "The cause of natural fluoridation is a base exchange process, the chemical agent involved in natural fluoridation being sodium fluoride."

There is also an account of the results of a dental survey of a sample of 56 children aged 9 to 15 years, in an area where the public water supply contains 2·5 p.p.m. of fluorine, to classify the extent of mottling present into the grades (devised by H. T. DEAN, *Fluorine and Dental Health*, Washington, 1942, Amer. Ass. Adv. Sci., p. 23), "normal", "questionable", "very mild", "mild", "moderate", "moderately severe" and "severe." The results were that only 2 children had mottling as pronounced as "moderate," 16 were normal and in 6 there were idiopathic spots. Some photographs of the anterior teeth of some of the children were compared with similar pictures taken 5 years earlier to ascertain whether changes in the degree of mottling had occurred. It is stated that dental inspections in the area where the fluoride concentration of the public water supply has been 2·5 p.p.m. for many years have never disclosed any disfigurement of teeth due to mottling. Only in some children who consumed water from wells containing 4·0 p.p.m. did white and brown stains appear which were obvious to the ordinary observer.

It is concluded that water naturally fluoridated at 2·5 p.p.m. brings about a 60% reduction in the incidence of caries and that the "mottling effects do not detract from the aesthetic appearance of the teeth." No adverse effects in the general health of the population could be discovered. *M. E. Delafield*

Sanitation

The order in this section is:—**General; Water and Swimming Baths; Sewage, Trade Waste and Refuse Disposal; Housing; Infestation; Atmospheric Pollution; Port, Ship and Aviation Hygiene.**

WATER AND SWIMMING BATHS

(Including the Bacteriology of Water Supplies)

METROPOLITAN WATER BOARD. **Thirty-Eighth Report on the Results of the Bacteriological, Chemical and Biological Examination of the London Waters for the Years 1957–1958** [TAYLOR, E. Windle, Director of Water Examination]. 116 pp., 13 figs. & 4 pls. [50 refs.] [1960.] London: New River Head, Rosebery Avenue, E.C.1. [21s.]

This, the 38th Report on the results of the bacteriological, chemical and biological examination of the London waters for the years 1957 and 1958, fully maintains the very high standard which previous reports have led one to expect. The record of routine and research work is clearly and interestingly written. In the introduction the Director of Water Examination says "The contents of this Report have altered through the years. Its preparation is now beyond the ability of one man to accomplish alone, because the work of the department has expanded, both in scope and variety. This publication has now become a collection of contributions by specialists on the staff devoting their time and energies to the various branches of water examination and treatment."

It is not possible to give more than a few indications of the wide range of the fields of work which are here described in considerable detail with a great number of tables of results.

Section II of the Report deals with the problems and anxieties in relation to the water of the upper River Lee because of the increased industrial activities particularly in Luton, the new satellite towns at Stevenage and Harlow and the growth of Welwyn and Hatfield. The measures taken have resulted in the waters of the upper River Lee being saved as a domestic water supply.

Radioactivity and the Board's Waters is the title of Section III in which there is a good account of radioactivity determinations of natural waters, rain water and treated waters. The Board has maintained the closest co-operation with the staff of the United Kingdom Atomic Energy Authority and the Radiochemical Inspector of the Ministry of Housing and Local Government. Up to the present such traces of strontium 90 as have been found are quite insignificant compared with the concentrations considered by competent authorities to be permissible.

The Bacteriological Section (Section IV) contains a report on the impressive amount of work done on routine and special investigations. Much progress has been made in improving the membrane filter method which "was adopted as the routine method for the enumeration of

coliform bacteria and *Escherichia coli* in all filtration works samples before chlorination from 1st January, 1958." Evidence of the excellent bacteriological quality of water passing into London supply is that of 11,594 samples of this water examined in 1958 the percentage negative for *E. coli* in 100 ml. was 99·96.

Among a number of investigations reported in the Chemical Section V, special work has been carried out on the examination of new biologically "soft" substances and other constituents of household synthetic detergents.

The Biological Section VI contains reports on the biological state of the principal storage reservoirs and rivers in 1957 and 1958, the performance of the micro-straining plant at the Lee Bridge works, the steps taken to cope with the midge nuisance particularly at Chingford, the control of pipe-encrusting mussels and the progress which has been made in the development of adequate limnological instruments for continuous observation and automatic control of the state of reservoir waters.

Epidemiological matters considered in Section VII include water-borne diseases, the methods of examination of employees, salmonella organisms in fertilizers in relation to the possible contamination of water, the detection of the flow of underground water by means of sodium phosphate, cesspools in the vicinity of wells and the control of rodents on waterworks premises.

Sections VIII and IX contain descriptions of new installations of apparatus which have been completed, incidents which have occurred and have led to problems; and a number of matters concerning the quality of water in the distribution system.

Section X is of particular interest as it is a 50 years review of complaints received regarding the quality of the supply. There is a good account of the method whereby every individual complaint is immediately investigated and a number of tables of detailed information. In 1958 there were 639 complaints which represents only 1 complaint per 187 million gallons supplied. There is an analysis under 22 headings of the different types of complaint of which the most numerous in 1958 were tastes and odours (240); rust, grit or sediment (104); cloudy, milky or chalky (69) and discoloured or dirty water (47).

Sections XI and XII cover (1) the effect of purification procedures on the fluoride content of water and (2) the results of experiment on the "filter skin" method for the clarification of river-derived water.

In addition to the numerous tables throughout this Report there is appended an index of subjects in the 30th–38th reports. [For 37th Report, see this *Bulletin*, 1958, v. 33, 1063.] *M. E. Delafield*

J. Amer. Water Works Ass. 1960, Mar., v. 52, No. 3, 301–7, 3 figs. **Status of Fluoridation in the United States and Canada, 1958. Report of Task Group 2620 P—Fluoridation Materials and Methods** [Phillips, R. S., Chairman].

The Task Group 2620 P, whose last report on fluoridation materials and methods in the United States and Canada in 1956 was published in 1957 [this *Bulletin*, 1958, v. 33, 253] here present an account of the developm of the fluoridation status in 1958. Statistics for the pe 1945–58, given in tables, show that the number of pe drinking water to which controlled amounts of fluo were added has increased in the United States from c 200,000 in 1945 to over 35 millions in 1958. number of fluoridated water supply systems in N America has increased from 4 in 1945 to 1,001 in 1 Figures of the number of water systems which have continued fluoridation are also given. It is stated that rate of increase of fluoridation in the United States declined, which has caused an official statement t "the proportion of the population not benefiting f this remarkable health measure is actually increasi

The fluoridation chemicals employed are mainly sod silicofluoride which is used in more than 50% of systems; sodium fluoride used by a large number of smaller systems and fluosilicic acid which is used in increasing number of small and large communities.

A sub-committee of the task group has been study a tentative standard for sodium silicofluoride and proposed a "feedability" index, based on particle s and water content, for comments on its value.

There is also an account of the more important c clusions of a detailed study by New York Univers during 1957–58 of water fluoridation in 20 major cities the United States [*ibid.*, 1960, v. 35, 102].

M. E. Delafiel

Arch. Indust. Health. Chicago. 1960, Apr., v. No. 4, 303–52, 4 figs. [27 refs.] **The Physiolo and Hygienic Aspects of the Absorption of organic Fluorides. A Symposium of Reports a Summaries of the More Recent Experimen Investigations on the Subject.**

In the foreword Dr. Robert A. Kehoe (University Cincinnati) who also writes an excellent short introd tion, states "This symposium had as its purpose the p sentation of general information on the hygienic aspe of the use of inorganic fluorides in industry, primari and in the wider field of the community, to a limi and secondary extent." It was designed "for the ben of a limited number of physicians, industrial hygie engineers, attorneys at law, and other technical personn who enrolled for formal post-graduate instruction in Institute of Industrial Health in this University."

This is a valuable and interesting symposium of papers and summaries of papers on recent scienti work on many aspects of the subject. Its scope is in cated by the titles, *viz.*:— *The Present Status of Den Research in the Study of Fluorides; Current Informati on the Quantities of Fluoride Found in Air, Food a Water; The Determination of Fluoride in Soft Tiss Bone and Urine; The Metabolism of Fluorides in Ma The Effects of the Absorption of Fluoride (8 paper Roentgenologic Findings in Fluoride Osteosclerosis; Su mary of Histopathologic and Chemical Findings, w Respect to Fluoride; The Significance of Time in Into cation of Domestic Animals by Fluoride; The Chemistr Histology and Roentgenology of the Teeth and Bones*

arge Animals; Investigation of Certain Hepatic Functons of Dairy Animals and *Notes on the Effects of Fluode Deposition on Body Tissues.*

The first communication is a summary of a report on ental surveys made in 3 districts in the United States in hich the communal water supplies have been fluoridated nce 1945. The promotion of dental health in this time clear. Topical application of fluoride, diet supplenents of fluoride and fluoride dentifrices are also disussed shortly.

There are short accounts of analytical procedures in hich the Megregian reagent (Zirconyl-eriochromeyanine R) is used which give satisfactory results with -5 μgm. of fluoride in certain materials. Some of the esults of analysis of air, food and water are given which ndicate the omnipresence of fluoride and the great variaions in its concentration.

On the subject of the metabolism of fluorides in man nere is an editorial summary of 4 papers published elsehere. Experiments in man have shown that:— (1) the bsorption by the alimentary tract of fluoride ingested in ne form of sodium fluoride, calcium fluoride, cryolite nd rock phosphate is remarkably effective, (2) roughly alf of the absorbed simple fluoride salts is excreted by ne urine and half is retained mainly in the skeleton, (3) odium fluoroborate while being readily absorbed (98%) s completely excreted by the urine and is not retained in ne body, (4) when the rate of intake and absorption of uoride is appreciably reduced the fluoride that has been etained in the skeleton is released slowly over a long eriod, (5) excretion of fluoride in sweat is a highly ignificant feature of its metabolism and (6) in general he human body tends to achieve a balance between the ntake and output of fluoride.

The section of this symposium which deals with the ffects of the absorption of fluoride contains 8 summaized reports on investigations on different facets of the ubject. (a) In a 10-year investigation of over 100 persons who for over 30 years had used water containing 8 p.p.m. of fluoride it was found that "no clinically significant, adverse, physiological, or functional effects resulted from the absorption of the fluoride, with the exception of some dental fluorosis," (b) study by X-ray of 546 persons aged 30–70 years in Framingham, Mass., where the water contains less than 0·1 p.p.m. of fluoride provided evidence that an insufficient amount of fluoride in adult bone is disadvantageous. Among various points in this evidence was the finding of 229 cases of osteoporosis, (c) several summaries of papers contain information on the findings of histological and chemical examination of human bone and soft tissues under variable conditions of fluoride ingestion.

Other papers deal with the important subject of fluoride intoxication in animals. In one of these papers there is a description, with references, of the results of experiments on induced clinical fluoride intoxication in animals in which there appears to be a species tolerance to the element. The tolerance in a given species is "modified downwards by factors of stress, such as infection, increased energy demands, shifts in certain dietary factors, and faulty nutrition." Another communication reports on the changes following prolonged feeding of fluoride to cattle and sheep from which it is concluded that dental fluorosis is an excellent clinical sign in the diagnosis of fluorosis in cattle and that definite radiological and histopathological changes have been observed in bone of cattle that contains 4,000 parts of fluoride per million. Studies of hepatic function in cattle by serum bilirubin concentration, sulphobromophthalein clearance and thymol turbidity tests showed that there was no indication of gross effect on liver function of ingestion of fluoride in concentration of 100 p.p.m. of the diet for a period of 5·5 years.

A short final paper contains notes on sources of fluoride, routes of entrance into the body, fluoride effects and a list of important, unanswered questions.

M. E. Delafield

SEWAGE, TRADE WASTE AND REFUSE DISPOSAL

MINISTRY OF HOUSING AND LOCAL GOVERNMENT. **Third Progress Report of the Standing Technical Committee on Synthetic Detergents** [CREMER, H. W., Chairman]. 18 pp., 1 folding map, 1 diagram & 2 figs. on 2 pls. 1960. London: H.M. Stationery Office. [1s. 6d.]

This is the third annual progress report of the Standng Technical Committee on Synthetic Detergents subnitted in accordance with the requirement of the terms of eference.

Examination of the data received up to October 1959 loes not reveal any pronounced change in the concenration of synthetic detergents at any of the sampling oints described in previous reports except that there has been some reduction in the River Lee. Foaming attriputed to these detergents continues to give rise to difficulties and complaints. The domestic and industrial consumption has continued to increase and this increase during the past 2 years has largely been due to a greater use of the detergents in liquid form.

Most of this report is devoted to an account of the year's research into 2 particular aspects of the problem of synthetic detergents—(1) the assessment by laboratory and full-scale experiments of the amenability to biological decomposition of an alternative alkyl benzene sulphonate produced by the industry and referred to in a previous report [this *Bulletin*, 1959, v. 34, 1147] and (2) the development of analytical methods capable of determining separately this new material and that now in general use when both are present in low concentration.

The new material which had been proved to be more amenable to biological oxidation ("biologically soft") in pilot scale sewage treatment plants was assessed, at the suggestion of the manufacturers, in a full-scale trial. This trial was and is being carried out at Luton and Harpenden with the full co-operation of the manufacturers who have as far as possible replaced the old

material with the new one in this area. There is a full description of the results of this trial and also of its difficulties and disappointments.

Nevertheless "Our tentative conclusions on the tests that have been carried out are that, while the new material is not completely removed during sewage treatment, its substitution for the material now in general would substantially diminish the troubles associated w synthetic detergents."

Analytical methods, based on infra-red spectrosc have been devised for determining the proportion of and new material in settled sewage.

M. E. Delafield

HOUSING

CHALKE, H. D., WATTON, R. W. & PENTNEY, B. H. **Assessment of Applications for Rehousing on Medical Grounds.** *Brit. Med. J.* 1960, Apr. 9, 1125–7.

This is from the Metropolitan Borough of Camberwell where Dr. Chalke is the Medical Officer of Health and Dr. Pentney is a general practitioner.

It is natural when there is a housing shortage that applicants should use every available means to advance themselves in the queue. The most popular is to obtain a medical certificate and it is the duty of the Medical Officer of Health to assess the urgency.

Between 1955 and 1958 the Borough Council received 3,235 applications for rehousing of which 1,623 claimed medical priority.

In such cases the applicant was required to sign a form which was first passed to a public health inspector who visited the house and filled in particulars of the accommodation, sanitary defects and whether there was any statutory overcrowding. The form was then passed to the general practitioner who was asked to state the illness from which the patient suffered, the housing features which affected it adversely and in which of the categories "most urgent," "urgent," "soon" or "no priority" the application should be placed. The co pleted form was not handed to the applicant but w posted by the doctor to the Medical Officer. The c tificates were reviewed by a panel of three, the Medi Officer of Health, a medical consultant and a gene practitioner, who made the final medical assessment. T assessment of the patient's doctor was "most urgent" 12·3% of the applications but it was reduced by panel to 6·9%: "no priority" was the decision by doctor in 10·6% and by the panel in 24%.

The most numerous, 19·9% of the total, as well as most difficult to assess, were the "functional nervous d orders"; the next most numerous were "bronchit 16·4%, and "tuberculosis," 14·4%; 35 of the 233 tub culous were given the highest priority by the panel a only 31 by the doctor supporting the application.

Even when a high priority cannot be given so exchanges of accommodation have been arranged w beneficial results.

The scheme works well. It has prevented applica from "shopping around" to collect a number of me cal certificates and enables the doctor to give a genu opinion if he thinks that there should be "no priorit without offending his patient.

Allen Dale

ATMOSPHERIC POLLUTION

MILLS, C. A. **Respiratory and Cardiac Deaths in Los Angeles Smogs during 1956, 1957 and 1958.** *Amer. J. Med. Sci.* 1960, Mar., v. 239, No. 3, 307–15.

In this paper the author continues his earlier studies [this *Bulletin*, 1957, v. 32, 777] of the relationship between cardio-respiratory mortality and smog in the Los Angeles metropolitan area. The present analysis covers the three calendar years 1956–58 and is based on data relating to (a) daily totals of mortality from respiratory and cardiac causes in Los Angeles County, (b) daily average of the highest oxidant concentrations recorded at some 15–20 stations in the area ,and (c) daily maximum temperatures obtained from Weather Bureau records. These data are presented in full for each of the years of the study.

Correlation coefficients of up to +·7 confirmed the close direct association between daily temperature and pollution levels in the Los Angeles environment. This association was evident at all seasons of the year and at daily temperature maxima ranging from 46°F to 104 The effect of pollution *per se* was assessed by analys deviations of daily mortality figures from monthly av ages in relation to concomitant oxidant levels. Aver deviations rose consistently from a *deficit* of −2 deaths per day at the 0 to 4 p.p.h.m. oxidant level to *excess* of 5·03 deaths per day with oxidant maxima 35 pphm or over. From this gradient and taking minimum pollution grouping (0 to 4 p.p.h.m.) as a b line the author estimates that the toll of excess card respiratory mortality directly associated with pollut amounted to 1,121 deaths over the 3-year period a suggests that the maximum allowable concentration total oxidant should not exceed 10 p.p.h.m. if the co munity health is not to be endangered.

[In assessing these results it is perhaps relevant remember that Los Angeles smogs have a different s sonal pattern from urban pollution in Britain, and re their peak in the hotter months of late summer and e autumn, *i.e.*, pollution is heaviest when seasonal morta is low rather than high.]

J. T. Boy

Occupational Hygiene

The order in this section is:—**General; Occupational Physiology; Occupational Diseases (Dust Diseases, Poisoning, Skin Diseases, Others); Occupational Psychology; Heating, Lighting and Ventilation.**

GENERAL

SINCLAIR, G. A. **A Morbidity Study on a Working Population.** *Canadian Med. Ass. J.* 1960, Feb. 20, v. 82, No. 8, 407–10.

In this report on a morbidity study the author states that in 1957 in his Company (Imperial Oil Ltd.) with a population of 14,773, there were 18,737 reported cases of absenteeism due to sickness which included injuries and there was a total of 126,895 calendar days lost from work. It is significant that 38·6% of the population lost no time. The 53% of the population that was absent 1, 2 or 3 times during the year accounted for 80·7% of calendar days lost. Then there is a small group of 8·4% of the Company population absent 4 or more times (4 to 19 times) that were responsible for 19·3% of calendar days lost.

The common practice of using morbidity statistics to inform management of the amount of existing sickness absences may unwittingly allow them to believe that those not having absences as sick cases are perfectly healthy. It was therefore decided to analyse periodic health examinations including pre-placement examinations for a period of one year, to determine the apparent health status of a working population. During the year 1957, 9,878 periodic and pre-placement examinations were completed, and 24,444 conditions or diseases noted —an average of 2·4 conditions per person examined. 12% of the conditions were newly discovered—that is, they were unknown to the employee before the examination. The remaining 88% of conditions were known to the employee and had in most cases been previously recorded. Included in this group were conditions that had been improved, corrected or controlled since a previous examination—33% of the total. Conditions that showed no change accounted for 49·5% of the total, and conditions that showed definite deterioration or relapse made up 5·5% of the total conditions.

No appreciable disease or abnormal condition was found in 15·6% of those examined.

It was observed that 1,866, or 13·2%, of the Company population could be considered as employees with limited work capacity. They were experienced employees who were able to do productive work when placed at suitable jobs within their physical and mental capabilities.

No evidence was found to support the contention that there is a high incidence of dermatitis in oil workers, but the Company has a high standard of factory housekeeping and the employees practice good personal hygiene. The incidence of diseases found is described.

P. J. R. Challen

BUGYI, B. Röntgenologische Reihenuntersuchung zur Früherfassung der Knochen- und Gelenkerkrankungen beruflicher-Genese. **[Serial X-Ray Examination for the Early Detection of Bone and Joint Lesions of Occupational Origin]** *Zent. f. Arbeitsmed. u. Arbeitsschutz.* 1960, May, v. 10, No. 5, 104–9. [23 refs.]

TOMASHEFSKI, J. F. & OLIVER, T. K., Jr. **Mouth-to-Mask Resuscitation.** *J. Amer. Med. Ass.* 1960, Apr. 23, v. 172, No. 17, 1888–90, 1 fig. [10 refs.]

Mouth-to-mouth resuscitation has been shown to be the most efficient method of emergency artificial respiration for the asphyxiated. The hygienic, aesthetic and possible hyperventilatory aspects of this technique are, however, still under consideration.

A mask has been devised which will permit direct insufflation to be performed and yet overcome these objections. By eliminating direct contact with the victim, the hygienic and aesthetic objections are removed, and hyperventilation is prevented by the operator re-breathing about 300 cc., of his previously exhaled air contained within the connecting tube between the operator's mouthpiece and the oro-nasal mask. A system of valves ensures that the operator does not re-breathe the victim's exhaled air and a pressure relief valve ensures that air pressures in excess of 24 mm. Hg cannot be applied to the victim.

It is again stressed that an unobstructed airway must be established and maintained at all times.

L. M. Croton

OCCUPATIONAL PHYSIOLOGY

BELDING, H. S., HERTIG, B. A. & RIEDESEL, M. L. **Laboratory Simulation of a Hot Industrial Job to find Effective Heat Stress and Resulting Physiologic Strain.** *Amer. Indust. Hyg. Ass. J.* 1960, Feb., v. 21, No. 1, 25–31, 1 fig.

For the assessment of the strain produced by work in a hot environment the best approach is to measure the circulatory responses, the body temperature, and the rate of sweating. But such direct measurement is not always feasible, especially in industrial situations, and then one

can try to predict the heat strain. A method of predicting heat stress by calculating the rate of heat-loss by evaporation necessary to maintain thermal equilibrium of the body was described by HAINES and HATCH [this *Bulletin*, 1953, v. 28, 442] and a system of grading the strain therefrom was suggested by BELDING and HATCH [this *Bulletin*, 1956, v. 31, 307]. Strictly, these predictions are only valid for persons who are nude or wearing at most one layer of very light clothing.

In the present paper the authors describe an attempt to use these methods to evaluate the heat stress and the resulting physiological strain for an industrial task involving exposure to radiant heat. During each 6-minute cycle of work the worker was exposed to a high level of radiant heat for 3 minutes, with mean radiant temperatures of 165 to 180°F., air temperatures of 120 to 125°F., and vapour pressures as high as 19 mm. Hg during hot weather. Working clothing was worn.

Calculations led to the conclusion that work under such conditions would result in severe overstrain, yet during the hot weather men had completed two 1·8 hour periods of exposure per shift without incurring injury. Clearly the calculations gave an over-estimate of the heat stress. It seemed likely that the discrepancy between prediction and experience was due to the clothing acting as a shield against the radiant heat, and to examine this point the task was simulated in the laboratory. Three young, acclimatized men worked in thermal conditions roughly similar to the factory environment, semi-nude, or wearing various assemblies of clothing.

It appeared that the ordinary working clothing shielded the subjects from about 30% to 40% of the radiant heat. The level of radiant heat used in the "clothed" experiments was intolerable when the subjects were semi-nude, and with a reduced intensity of radiation the subjects suffered significantly more strain when they were semi-nude than when they were clothed.

Experiments were made with metallic-coated, heat-reflective clothing. Although such clothing gives increased protection from radiant heat, it may interfere seriously with the evaporation of sweat. If such clothing is to be worn for prolonged periods the design must provide for good ventilation so that evaporation is not hindered; otherwise the heat strain may be greater than with ordinary working clothing.

Thomas Bedford

BROUHA, L. **Effects of Muscular Work and Heat the Cardiovascular System.** *Indust. Med. & Surgery.* Chicago. 1960, Mar., v. 29, No. 3, 114–2 7 figs.

Muscular activity and heat are both factors that c create exceptional conditions of stress and tax the cardi vascular system to its maximum capacity. Work itself can strain the homeostatic mechanisms to th upper limits and lead to complete exhaustion, as in at letic competitions. When heat stress is also present t maximum reactions attainable remain the same, but th are reached with less work and in a shorter time. Su conditions arise when hard work is carried out in h weather or in some industrial situations.

The cardiovascular system reacts to muscular wo and to heat exposure by an increased cardiac output a a redistribution of the blood flow according to the nee of the various organs. When no heat stress is involv most of the blood is available to transport oxygen to t working muscles, and maximum oxygen intake and ma mum performance are attainable. When heat stress present an important part of the total blood volume mu be used for the purposes of thermoregulation, and ma mum oxygen intake can no longer be achieved. Th the maximum heart rate and cardiac output are reach sooner, and the working capacity is reduced as t environmental temperature rises.

In most instances the heart rate is an accurate ind of cardiovascular stress. The heart rate is affected high ambient temperatures during work and during t period of recovery from work, and the physiologic strain can be assessed from measurements of the hea rate during work and in the period immediately after The use of heart-rate recovery curves for evaluating t effects of work, heat and individual fitness is a simp and useful method in field research.

When an industrial job has been recognized as cau ing high reactions because of either the work load or t heat exposure, or of both, improvements can be soug and these should be evaluated in terms of physiologic values until a satisfactory solution is found. In indu trial situations heat is often the major cause of stress a of low productivity. Adequate measures to combat he are available, and suitable measures should be adopte

Thomas Bedford

OCCUPATIONAL DISEASES

DRASCHE, H. Zur Frage der Staubgefährdung in den Sinteranlagen saarländischer Eisenhüttenwerke. [**Dust Hazard in Sinter Plants in Saar Iron Foundries**] *Arch. f. Gewerbepath. u. Gewerbehyg.* 1959, v. 16, No. 6, 666–96, 11 figs. [Numerous refs.]

All the workers in 4 sinter plants who had worked in these plants for more than 9 years were investigated. Those who had a history of other forms of dust exposure were excluded and chest X-ray examinations were made of the remainder. The atmosphere in the sinter plants was sampled by the konimeter, thermal precip tator and the cyclone. Each X-ray film was read sepa ately by 5 readers experienced in silicosis. 140 worke were investigated and compared with 216 high ov workers. 60% of the sinter plant workers were ag 46–60 years and the oven workers were of a similar a range. On the whole most of the sinter workers h shorter histories for their occupation than the ov workers. Of the sinter workers 28 showed radiologic changes of pneumoconiosis and there was a good cor lation between incidence of radiological change and ye

exposure to dust. The radiological changes were simi- r to those seen in coalworkers. The authors also vestigated the comparative incidence of upper respir- ory infection in the sinter plant and high oven workers; ckness absence due to upper respiratory infection dur- g the year 1956 for sinter workers was about double at for high oven workers. There was also a high cidence of sinus infection in the sinter plant workers. adiological changes, with few exceptions, were seen in ose who had 25 years' exposure to dust in the sinter lant. Chemical analysis of the dust showed it to con- in 40–45% iron oxide with 1–2% free silica. Most of ie dust particles were below 5 microns in size. The uthors consider the radiological changes as those of a ight silicosis. *D. Rivers*

VINDER, G. E. **An Automatic Continuous Sampler for Airborne Dust.** *Safety in Mines Research Establishment.* [Portobello St., Sheffield, 1.] *Research Rept.* No. 184. 1960, Feb., 16 mimeographed pp., 11 figs. [2s.]

VYSS, V. & PETTINATI, L. Tecnica pratica di conteggio delle particelle di polvere raccolte con precipitatore termico. **[The Counting of Dust Particles collected with the Thermal Precipitator]** *Rass. Med. Indust.* Rome. 1959, Nov.–Dec., v. 28, No. 6, 447–63, 2 figs. English summary.

The authors state that with the usual procedures errors n counting dust particles collected by the thermal pre- ipitator are frequent by reason of the varying magnifi- ation used and depending on whether an illuminated, or dark field is used, the error being much greater with he latter especially as regards particles 1μ or less and ven those $1–2\mu$ in size.

They then describe a procedure in which illumination s provided by a mercury vapour lamp with a green ilter, a photographic negative being thrown onto a erspex screen 48 × 60 cm., the final figure then magni- ied by 10 and the particles counted by automatic ounter.

Comparison of this procedure (a), with a microscopic icture × 200 on a clear field (b), and by a *positive* hotographic arrangement × 200 (c), showed that with a) nearly 4 times as many particles were counted as with b) and 37% more than with (c) though the relative error of the 3 methods only varied from 20·2 to 29%. As, owever, this was much too high, a second series of tests vas made with samples having a much lower dust con- ent; here the error at the 5% level was very much less with (a). The authors emphasize the fundamental mportance of the granulometric size of the particles and conclude (1) that the method described gives very much igher counts than either of the other 2 procedures; (2) he usual microscopic method leaves out nearly all the particles $<1\mu$ and even some of $1–2\mu$; (3) the advantages of their method are greater magnification and conveni- ence for those counting; (4) the relative error is then reduced to about ± 12–15%. *W. K. Dunscombe*

SCHLIPKÖTER, H. W., STEIGER, H., BECK, E. G. & ESSER, H. F. Elektronenmikroskopische Untersuchungen der atmosphärischen Luftverunreinigungen und des Schwebestaubes in Bergwerken. **[Research with the Electron Microscope upon Atmospheric Pollution and Airborne Dust in Mines]** *Ztschr. f. Hyg. u. Infektionskr.* 1960, v. 146. No. 3, 267–75, 7 figs. [11 refs.]

A sampling system is described which is suitable for particles below 0·5 micron diameter and uses membrane filters. It is considered that the usual method of dissolving the filter in acetone may permit coagulation of the deposited particles. This artefact is avoided by placing the filter, dust side down, in contact with the silica-coated formvar film of the electron microscope specimen-holder, which is held in a float, and irrigating it carefully from below in a special apparatus. In this manner complete solution of the membrane filter is effected and the dust particles are transferred to the film without change of position or coagulation.

Samples taken in coal mines revealed that the particles which became airborne during coal-getting had a size distribution with two moderate peaks at 0·2 micron and at 5 microns. In contrast, pneumatic stowing produced a high concentration of dust with most particles below 1 micron. Comparison with the particle-content of the outside atmosphere drawn into the mine for ventilation showed clearly that the smallest particles in the mine air, below 0·5 micron, were produced by pneumatic stowing.

Dust raised by shot-firing in rock was finer than that from coal-getting but not so fine as dust produced during pneumatic stowing. The size-distribution had a sharp peak at about 0·5 micron diameter.

Samples of the atmosphere were also taken in two cities. Size distributions are given showing many particles smaller than 0·1 micron diameter, with similar size distribution in both the city and harbour areas of Dusseldorf. The air of Bochum contained fewer fine particles but the distribution curve rose from 1 to 0·05 micron. *C. N. Davies*

LICHT, W. Zur Deutung zwei verschiedener Kurventypen bei der Adsorption von Serumeiweissen an Quarz. **[On the Interpretation of Two Different Types of Curve representing Protein Adsorption on Quartz]** *Arch. f. Hyg. u. Bakt.* 1960, Mar., v. 144, No. 2, 127–36, 6 figs. [10 refs.]

Previous work [this *Bulletin,* 1958, v. 35, 48] had shown that when protein adsorption by quartz after contact with different samples of human or bovine serum was measured at *p*H 3, 5·2 and 9, there was either increasing adsorption as *p*H was lowered (type I curve) or there was an adsorption peak at *p*H 5·2 (type II curve). Adsorption was measured by determining the amount of nitrogen remaining on the quartz after repeated washing with saline until tests with sulphosalicylic acid showed freedom from protein. The protein concentrations had varied widely with different serum samples and the levels of adsorption had also varied.

The present paper describes a series of tests designed to explain the previous results. One particular quartz sample was used throughout at a standard concentration (1 gm. in 2 ml. medium) and human and bovine sera were diluted to have equal protein contents. It was found that the levels of total protein adsorbed were much more similar than before, but the previously observed differences still occurred; out of 3 sera 2 showed curve II type and one curve I type.

The relation between adsorption level and stability of colloidal solution was tested by adding to the sera protamine, which reduces, and heparin or eosin, which increase the stability of the protein against heat denaturation after addition of variable amounts of calcium chloride.

A serum showing curve type I could be changed to type II by adding protamine, and a number of further tests showed an inverse relation between colloid stability and adsorption level.

There is a long and rather speculative discussion of these results. It is suggested that a part of the so-called "adsorption" on quartz is really a precipitation of labile colloidal protein, and histones which are related to protamine are said to be perhaps involved in the silicotic tissue reaction. *G. Nagelschmidt*

ELYASHEV, L. I. **[Pneumoconiosis among Bauxite Miners]** *Gigiena Truda i Professional'nye Zabolevaniya.* Moscow. 1960, v. 4, No. 4, 28–32, 3 figs. on 2 pls. [15 refs.] [In Russian.]

The English summary appended to the paper is as follows:—

"To ascertain the incidence-rate of pneumoconiosis among miners exposed to bauxite dust—105 of them in the age group of up to 45 years, with a total underground-work record of from 5 to 10 years, were subject of a special examination at one of the bauxite mines in the northern Urals. Chemical analysis of bauxite ore showed the level of SiO_2 to be within the range of 4·8–7·22%, that of Al_2O_3—from 77·46% up to 81%, and of Fe_2O_3—from 3·5 up to 8·73% Microscopic investigations confirmed the silica (SiO_2) to be in a combined state.

"The above study made it possible to establish that dust-occasioned changes in the lungs, consequent upon the bauxite ore aerosols action, are distinguished by non-acute pulmonary fibrosis and basal emphysema. These can be discovered predominantly by roentgenological means and, as a rule, fail to produce any clinical manifestations. Main symptoms of a typical pneumoconiosis are actually absent.

"A singular clinico-roentgenological picture was revealed in the workers who prior to the bauxite had been engaged at some other mining enterprises, notably in those extracting such minerals as gold and copper. In this instance, the pathology differs from the changes wrought by the inhalation of bauxite dust alone, and from the picture of a typical silicosis.

"The dust-occasioned fibrosis in bauxite miners differs both from aluminosis produced by metal dust and from the pulmonary changes caused by bauxite smoke formed during manufacture of aluminic abrasives. This indicates that aerosols of one and the same mineral or m can call forth varying clinico-roentgenological forms dust-caused pulmonary pathology."

FRIGERIO, G., HENKING, E. & OCCELLA, E. Il risc silicotigeno nel lavoro dei muratori ai forni Ma delle acciaierie. **[Silicosis Hazards in the W of Open Hearth Furnace Bricklayers]** *Med. Lavoro.* 1960, Jan., v. 51, No. 1, 68–75, 1 English summary.

This is a report by a physicist and 2 engineers. T point out that the refractory materials of which o hearth furnaces and the requisite pre-heating and pc ing ducts are composed consist of both acid and ba refractories. These refractory bricks slowly become rified and have to be renewed every few months. they have a high Si content there is a potential risk silicosis, since the work of the bricklayers consists in regular demolition and reconstruction of the refract portions of these furnaces, work which generally ta rather less than 2 weeks at a time.

4 steelworks in northern Italy were investigated regards this demolition and reconstruction procedure, dust content of the atmosphere at certain sites in works, the particle size, and estimation of the free present, etc. In general, while the works were functi ing the dust content was not high, though as might expected "knocking-out" and cleaning of the mou caused a marked rise in the dust content so that the f crystalline Si particles present exceeded the MAC (10 cc.air). The area around the ingot section presente notable silicosis risk though only for limited periods a time. The operatives at the open-hearth furnaces the selves were exposed to considerable amounts of dust the silicosis risk was not excessive. However an int esting finding was that in the cabin of the transpor crane there was a very large number of particles betw 0·6 and 5μ, mostly $<1\mu$, hence this cabin can be a pot tial danger.

The authors conclude (a) in steelworks 65–85% of dust content is formed by particles $<1\mu$, the Si cont varying between 1·1 and 22%, (b) the Si is in the fc of quartz, tridymite, or crystobalite, (c) in general in st works there is not a grave risk of silicosis except knocking-out, the ingot section, the crane cabin, and the manual removal of the acid refractory surface of open-hearth furnaces and (d) in the reconstruction such furnaces the free crystalline Si is higher than wl the furnace is in operation. *W. K. Dunscomb*

SCHUDEL, W. Studien zur Beziehung zwischen Giesse Silikose und Tuberkulose. **[A Study of the Re tion between Silicosis and Tuberculosis in Foundry]** *Arch. f. Gewerbepath. u. Gewerbeh* 1960, v. 17, No. 6, 643–50, 2 figs. [15 refs.]

This is a statistical study similar to a previous one BERTSCHI and STIEFEL [this *Bulletin*, 1951, v. 26, 7 The population of a large foundry was divided into th

exposed to quartz dust (fettlers, formers, core makers, etc.) and others not exposed to quartz dust.

All cases of tuberculosis occurring between 1945 and 1956 were tabulated with the following results:

		No. of men	Tb	%
This study:	exposed	1582	84	5·3
	not exposed ...	3901	90	2·3
	total	5483	174	3·2
Previous study:	exposed ...	1600	49	3·1
	not exposed	5700	113	2·0
	total	7300	162	2·2

The attack rate of tuberculosis was higher for men exposed to quartz dust. Similar figures were obtained from mass radiography surveys, where the foundry population gave 3·2% of new tuberculosis cases as against 1·6% for other industries in the neighbourhood.

An analysis of the age distribution showed that in the quartz-exposed group there were many more cases of tuberculosis in men over 45 years of age and fewer in men under 20 years than in the group without a quartz risk. Average length of sickness absence due to tuberculosis was about equal for both groups, 16 and 15·5 months. Pleuropulmonary forms of tuberculosis were 98% for the exposed as against 83% for men not exposed.

40 of the 84 men with tuberculosis had less than 10 years' dust exposure before the onset of tuberculosis and this is taken as evidence that even small amounts of quartz may increase the liability to contract tuberculosis, well before there is any X-ray evidence of silicosis.

G. Nagelschmidt

KHVAPIL, M. **[Biochemical Methods in Assessing the Effect of Industrial Dust on the Organism]** *Gigiena Truda i Professional'nye Zabolevaniya.* Moscow. 1960, v. 4, No. 4, 33–8, 2 figs. [18 refs.] [In Russian.]

The English summary appended to the paper is as follows:—

"Experimental silicosis in rats was produced by intratracheal administration of SiO_2 in mice—by intravenous introduction of 0·5 mg. dust suspension in a saline solution, and also by the lung tissue cultures of 14-days-old chick embryos.

"To evaluate the extent of fibrotic effect exercised by SiO_2—various methods of collagen proteins (hydroxyprolin) estimation were used. Particular importance is attached to the determination of soluble forms of collagen proteins in the dynamics of the pathological process. The paper carries detailed characteristics of the methods employed and of the results actually obtained.

"Verification of diverse procedures used for the estimation of collagen proteins in the biological material proved that in the instance of lung tissues, the most suitable one is that of direct hydroxyprolin estimation in the intact native tissue.

"The above research opened up the way for possible use of lung culture technique in quantitative observations of fibroblasts reactions to the dust undergoing investigation."

SCANSETTI, G. & BRAJA, M. Osservazioni su alcune proprietà fisiche dei polmoni nelle pneumoconiosi. **[Remarks concerning certain Physical Properties of the Lungs in the Pneumoconioses]** *Rass. Med. Indust.* Rome. 1959, Nov.–Dec., v. 28, No. 6, 464–83. [Numerous refs.]

The English summary appended to the paper is as follows:—

"The authors expound the principles of respiratory physiology and the laws of general physics applicable to the study and interpretation of pulmonary mechanics, with special consideration to the elastic properties of the lung and to the resistance of the airways and of the lung tissue. They report on the presupposition and practice of the principal methods which can be used for the determination of lung compliance and resistance.

"Based on 333 lung compliance tests conducted on normal subjects, the authors show the average values of lung compliance (0·205 liters/cm. H_2O), total non elastic lung resistance (1·20 cm. H_2O/liter/sec.), resistance of the airways (0·99 cm. H_2O/liter/sec.) and tissue resistance (0·21 cm. H_2O/liter/sec.).

"In pulmonary silicosis the value of lung compliance averages 0·173 liters/cm. H_2O, while in asbestosis and anthracosis the values are even lower, respectively 0·066 and 0·138 liters/cm. H_2O. The authors discuss the factors which may determine the particular elastic behaviour of the pneumoconiotic lung, stressing in particular the importance of the various forms of emphysema, as regards silicosis.

"Although it is impossible, because of the insufficient experimental evidence now available with respect to both compliance and, even more, lung resistance, to trace a precise picture of the mechanical behaviour of the lung in pneumoconioses and to thorougly discuss its pathogenesis, the authors stress the importance, in occupational medicine, of the study of the physical properties of the organ of respiration, because of its value as a tool of diagnosis and medico-legal investigation, and because of the objectivity and reliability of the data it supplies."

SCHLIPKÖTER, H. W. & LINDNER, E. Submikroskopische Membranstrukturen in silikotischen Quarzgranulomen der Rattenlunge. **[Submicroscopic Membranes in Silicotic Granulomas in the Lungs of the Rat]** *Ztschr. f. Hyg. u. Infektionskr.* 1959, v. 145, No. 6, 574–86, 7 figs. [Numerous refs.]

Female rats were given 50 mgm. quartz dust by intratracheal injection and killed 9 months later. The lungs showed well collagenized acellular lesions many of which were confluent. Sections of these lesions were fixed in 1% osmic acid on palladium for 4 hours at 4°C., washed in ethyl alcohol and embedded in butyl methacrylate. Electron microscopy revealed concentric lamellated membranous structures which consisted of interwoven lattice

layers. These membranous structures formed thick aggregates arranged in reticular, lattice, concentric, dendritic and irregular formations. It is suggested that these structures possibly originate from an interaction of quartz with proteins such as muco- or gluco-proteins and lipids. *D. Rivers*

FERIN, J. & ÚLEHLOVÁ, V. Über die Selbstreinigung der Lunge von Staub und ihre Bestimmung im Tierversuch. [**Elimination of Dust from the Lungs and its Estimation in Animals**] *Arch. f. Gewerbepath. u. Gewerbehyg.* 1959, v. 16, No. 6, 630–43. [Numerous refs.]

The authors gave one group of rats 70 mgm. of quartz dust and to another group they gave 50 mgm. of dust. Previous experiments had shown that after intratracheal injection of 70 mgm. a mean value of 47·45 mgm. of quartz is found in the lungs immediately after the injection; for an injection of 50 mgm. a mean value of 26·3 mgm. is found in the lungs immediately after injection.

Rats were divided into 2 groups; one group received 70 mgm. and the other 50 mgm. quartz by intratracheal injection and groups of 4-5 were killed immediately after the injection, and then 3 days, 10 days, and 20 days after injection. There was no elimination in the first 3 days in the 70 mgm. dose group and only 5% was eliminated on the 10th day after injection; about 16% was eliminated by the 20th day. For the 50 mgm. dose group about 10% was eliminated by the 10th day and by the 20th day only 17% was found to be eliminated. In a series of experiments to test the effect of cortisone on dust elimination from the lungs one group of rats received 2 mgm. corticotrophin 3 times weekly and another group received 5 mgm. corticotrophin 5 times weekly. Both groups of rats had first received intratracheal injection of quartz dust and were killed 20 days after this injection. Corticotrophin was found to accelerate elimination of dust; 36% [shown in the text as 26%] was removed in 20 days in the group which received 2 mgm. corticotrophin whereas only 13% were eliminated in the same period in a control group which received no corticotrophin. The 5 mgm. dose of corticotrophin did not influence dust elimination. The results suggest that some means can be found for increasing elimination of dust from the lungs. *D. Rivers*

ANTWEILER, H. Mastzellen und Histamin nach Injektion von Staubsuspensionen. [**Mast Cells and Histamine after Injection of Dust Suspensions**] *Arch. f. Gewerbepath. u. Gewerbehyg.* 1959, v. 16, No. 6, 607–19, 5 figs. [Numerous refs.]

A series of experiments was performed to investigate the comparative effects of either intraperitoneal or intratracheal injections into rats of various dusts suspended in different media such as distilled water, Tyrode solution, Ringer solution, 0·95% sodium chloride, and 5·25% dextrose. Distilled water alone caused disruption of mast cells with subsequent release of histamine. The ionic content of the suspension medium was also found to be related to the number of mast cells disrupted and t amount of histamine released. Dust particles rapi adsorbed histamine and the amount so adsorbed depe ded both on particle size and on nature of the du Coal adsorbed histamine more rapidly and more firm than quartz. The nature of the suspension medi could be an important variable affecting the intensity the tissue reaction to any dust suspended in that mediu The results of these experiments suggest that distill water and substances such as dextrose should not be us in experimental pneumoconiosis. *D. Rivers*

HASSELT: INSTITUT D'HYGIÈNE DES MINES. Commu cation No. 165. Contrôle de l'efficacité des masq anti-poussières. Application de nouvelles norm d'agréation (cinquième série d'essais) [**Control the Efficiency of Dust Respirators. New Sta dards of Acceptance (Fifth Series of Trials** [DEGUELDRE, G.]. 1959, Nov. 15, v. 14, No. 8, mimeographed pp., 8 pls.

Out of 53 types of dust respirator tested between 19 and 1956, 14 were found acceptable on the basis of c tain standards. It was argued that, although these mig be adequate for selecting respirators for use in the co industry, more rigorous standards were necessary, in t presence of quartz dust.

The following new standards of acceptance were ther fore instituted: *Dust retaining power,* not less than 95 as measured by the tyndallometer after 3 hours test on breathing machine operating 26 respirations of 1·6 litr per minute. The dust is quartz with all particles belo 5 microns and 60% below 1 micron diameter; *resistan* including valves, etc., on exhalation below 5 mm. wat gauge, and on inhalation 10 mm. when new and 15 m after 1½ hours of use under standard conditions; *a tightness,* less than 25 cm.³ per minute leakage with pressure deficit of 35 mm. water gauge inside the mas *interior volume* not more than 150 cm.³; *weight,* belo 250 gm.

Brief descriptions are given of 41 commercially ava able dust respirators which were tested. Of these were satisfactory in all respects and are shown in ill strations. They are placed in three lists in order merit with respect to expiratory resistance, dust filteri efficiency and inspiratory resistance. *C. N. Davies*

[For 4 previous series see this *Bulletin,* 1954, v. 29, 4 *bis*; 1955, v. 30, 688; 1956, v. 31, 1237.]

VYSKOCIL, J., SKLENSKÝ, B., CHVAPIL, M. & POLÁK, Der Einfluss von Aerosolinhalationen auf durch gemischten Kohlen- und Quarzstaub veru sachte Staublunge bei Ratten. [**The Effect Inhalation of Aerosol on the Pneumoconio produced in Rats by Inhalation of Mixed Du containing Coal and Quartz**] *Arch. f. Gewerb path. u. Gewerbehyg.* 1960, v. 17, No. 6, 627– 9 figs. [23 refs.]

This is an experiment undertaken to test the effecti ness of prophylactic aerosol inhalations for men expos

o a dust risk. Such inhalations were widely practised n Germany a few years ago and were also recommended y Dautrebande.

Two experiments are described. In a preliminary run 6 rats were exposed in a rotating chamber for 5 minutes o a coal dust cloud containing 7·5% of quartz. Half he rats were subsequently allowed to inhale an aerosol f spa water from Vincentka. The main constituent of his is 10% $CaCl_2$; it also contains bicarbonate of odium and calcium, and iodine. The rats were killed ½ hours, 2 days and 7 days after the single dust inhalaion.

In the main experiment there were 15 rats in each of groups; exposure to dust with 7·5% of quartz (2 roups) and with 12½% quartz (2 groups) were given twice nd later once weekly (again for 5 minutes) for 4 months, oth with and without subsequent daily 30-minute aerosol nhalation. The fifth group was a control group which as not dusted and did not inhale aerosol. All animals n the 5 groups were killed 20 days after the last dusting eriod.

The results were evaluated by histological examination f the right lungs and by biochemical analysis of the left ungs. Total lung weight, hydroxyproline (HyPro) and cid mucopolysaccharides were determined; HyPro by hvapil's method (*Beiträge Z. Silikose Forschung*, 1960, . 64), the polysaccharides as hexosamine by the method f Blix (*Act. Chem. Scand.*, 1958, v. 2, 467).

The preliminary run with one single dusting period howed, 1½ hours after inhalation, plenty of dust in rachea, bronchi and in the lungs, but no difference with r without aerosol inhalation. Some of the dust was nside phagocytes. After 2 and 7 days there was less ust in the lungs and aerosol inhalation seemed to favour ust removal.

The histological changes after the main experiment (4½ nonths) are described in detail and eight illustrations are iven.

Dust was collected mainly around the respiratory ronchioles, there was some perifocal emphysema, and he lymph glands contained dust but no fibrosis could be ound by van Gieson or Gömöry staining in lungs or glands. The impression was gained that the amounts of dust were equal in all 4 treated groups but the dust was collected in larger aggregations and less of it was diffusely distributed in the lungs of the rats which had been given aerosol after dust inhalation.

The biochemical results are given as averages and standard errors in a table and here significant differences were found. The dust with the lower quartz concentration when inhaled without aerosol gave significantly increased lung weight and HyPro as compared with the controls and the amount of hexosamine was doubled. The same dust with aerosol inhalation gave actually less lung weight and HyPro than the controls but hexosamine was just as high as in the dusted group without aerosol. The dust with the higher quartz content also gave significant increases in lung weight, HyPro and hexosamine when compared with the controls but here there was no difference between the groups with and without aerosol.

In discussing these results, the authors point out that it is reasonable to find biochemical changes earlier than histological changes (collagen fibrosis). They believe that the challenge due to the dust with 12·5% of quartz was too strong to be counteracted by aerosol, whereas the effects of the dust with 7·5% of quartz were considerably diminished by aerosol treatment. Whether this was due to increase in dust elimination or whether the fibrogenic activity of the fibroblasts (?) was decreased cannot as yet be stated. Further experiments are said to be necessary before recommendations about the use of aerosol inhalation in industrial practice can be made.

G. Nagelschmidt

Walkenhorst, W., Beckmann, H. & Dautrebande, L. Weitere Ergebnisse bei der Anwendung von Kochsalz-Aerosol in einer Steinkohlenzeche. [**Further Results Obtained with Sodium Chloride Aerosol in a Coalmine**] *Beiträge z. Silikose-Forschung.* 1960, No. 65, 1–25, 9 figs.

The English summary appended to the paper is as follows:—

"The present paper reports some results obtained in the course of field experiments performed in order to determine the influence of a micromicellar aerosol of about 1% NaCl on the size of the dust particles in a coal mine. The aerosols were produced by means of generators functioning according to the principle of obligatory liquid filtration described by Dautrebande; these aerosols were produced at a distance of 660 to 95 meters from the working place and the dust measurements took place simultaneously at different places of the face and at the top of the extraction gallery, immediately in front of the return airway. As in previous papers, Walkenhorst thermal precipitators fitted with sedimentation tubes, 20 and 40 cm in length and 1 cm inner diameter, were used for air sampling. These tubes were destined to determine the influence of the NaCl agglutination on the sedimentation rate of the dust particles, first at normal underground relative humidity and then in an air saturated with water vapour up to 99,5%. This second series of experiments at very high relative humidity was done in order to simulate the conditions encountered by the "dust-NaCl" aggregates when reaching the upper respiratory tract. Under these conditions, it was regularly observed that the sodium chloride aggregates settle down much quicker than the dust particles alone. Moreover, it was constantly observed that in presence of NaCl-aerosols, the number of fine dust particles diminished significantly, this being in accordance with a previous paper published in 1954.

"This decrease of the number of fine dust particles in presence of NaCl-aerosols was found to vary from 25 to 36% for dust particles less than 2 microns and from 40 to 45% for dust particles less than 1,35 micron in size.

"It is therefore established that sodium-chloride underground aerosolation diminishes the number of fine dust particles which normally are deposited in the deep parts of the lungs. Therefore one is justified to employ these aerosols as a means of controlling silicosis.

"Incidentally a simple device is described, permitting to replace in clean atmosphere the sampling plugs of the thermal precipitators underground."

DAUTREBANDE, L., BECKMANN, H. & WALKENHORST, W. Untersuchungen über die verstärkte Abscheidung von Staub-Kochsalz-Aggregaten in den oberen Atemwegen des Menschen. [**Studies on the Increased Deposition of Dust and Sodium Chloride Aggregates in the Upper Respiratory Tract in Man**] *Beiträge z. Silikose-Forschung.* 1960, No. 65, 27–49, 9 figs. [20 refs.]

The English summary appended to the paper is as follows:—

"1. When a sodium chloride aerosol composed of small particles (mean count diameter 0·03 to 0·04μ) is coagulated in air with coal dust particles (mean diameter 0·7 to 0·8μ), the deposition of dust in the airways is increased regardless of the frequency (3 to 32 per minute) and of the tidal volume (350 to 2500 ml.) of the respiration.

"2. In air with a relative humidity below 60%, salt crystals which form aggregates with dust do not appreciably increase the size of the dust particles. However, when these aggregates penetrate into the respiratory passages, their size increases considerably and immediately. This leads to an increased deposition of dust particles in the form of aggregates in the conducting airways. This early deposition prevents the penetration of some of the fine dust particles into the deep parts of the lungs. This, in conjunction with earlier experiments on animals, leads us to suppose that such early deposition of the dust in the inspired air can weaken the harmful (functional and organic) effects which these particles normally produce when they reach the alveolar regions of the lungs."

KARAJOVIC, D., POTKONJAK, V. & GOSPAVIC, J. Die Silikoantimonose. [**On Silico-antimonosis**] *Arch. f. Gewerbepath. u. Gewerbehyg.* 1960, v. 17, No. 6, 651–65, 11 figs.

There has been since the end of the war a rapid increase in industrial activity in Yugoslavia, accompanied by an increase in industrial diseases. As most of the new cases of pneumoconiosis were found in miners of antimony, copper, lead and coal, a detailed study of a mine producing antimony and of a smelter plant processing the ore was undertaken. The results of this medical and environmental study are presented in the paper.

Mining conditions were poor. The mine was unmechanized, poorly ventilated and until 2 years ago all drilling had been dry. The quartz content of the rocks varied between 6·8 and 76·2%. A radiographic survey among 400 workers showed over 20% with silicosis stages I–III, and silico-tuberculosis, and 25% with stage 0-I after 3 to 8 years of dust exposure.

According to the Sidney classification the X-rays were those of simple (micronodular or nodular) pneumoconiosis or massive fibrosis, often complicated by tuberculosis. 3 X-rays are reproduced.

The operation of the smelter is described briefly; the ore, a sulphide of antimony, is ground and oxidized in a rotary furnace, the volatile oxide is collected and reduced and refined in other furnaces. Much dust is developed which consists mainly of Sb_2O_3 with up to 7% of quartz and 0·3–9% of As_2O_3. Thermal precipitator counts ranged from about 2,000 to 12,000 p.p.cc., mostly of s below 0·5 micron.

X-ray examination of 101 smelter workers showed doubtful and 14 definite cases of simple pneumoconios and a number of category 3 X-rays are reproduc These were pinhead or micronodular and could thus differentiated from those of the miners. They develop more slowly than in the miners. 8 smelter men bel the age of 40 were found to have emphysema and bro chitis. Toxic effects due to arsenic or antimony w not found but there were several cases of dermatitis d to antimony.

Lung function tests (indirect MBC, vital capacity a reserve air) on 20 smelter workers with X-ray abnorma ties showed slight insufficiency in 10 and definite ins ficiency in 1 of them. PMF has so far not been observ among the smelter workers.

The X-ray pictures, especially of the smelter worke are said to resemble those seen in iron ore workers Germany, France, Britain and in coal workers fr South Wales. The name silico-antimonosis is propos to characterize this condition. *G. Nagelschmid*

PUCCINI, C. Il problema della cancro-silicosi. [**T Problem of Cancer-Silicosis**] *Med. d. Lavo* 1960, Jan., v. 51, No. 1, 18–36, 1 fig. [Numerc refs.]

The English summary appended to the paper is follows:—

"The problem of pathogenetic relationship betwe silicosis and primary bronchial or lung carcinoma ca not be approached and solved only through statisti and experimental studies, but it must be investiga considering the whole complex of several factors wh form a pathogenetic sequence. Recent new viewpoi suggest that environmental pollution with silica dust c be one of several exogenous factors responsible for t increased incidence of bronchial and lung carcinon The hypothesis of protective action of silicosis agai neoplasia by a blocking action on lung cancer was n demonstrated, while the action of silicosis in favouri the growth of lung carcinoma can be documen through such reactions as pathologic epithelial regene tion (hyperplastic, dyplastic, metaplastic) and profou tissue disorganisation (cellular dislocation, alteration the epithelial-stromal connections), which are induced lung tissues by pneumoconiosis and may represent starting point for neoplastic growth. The diffuse t dency to deny any importance of silicosis in carcin genesis must therefore be revised, particularly in vi of compensation for cases of cancer-silicosis."

BOUHUYS, A. **Byssinosis.** *Nederl. Tijdschr. v. Genee* 1959, Nov. 21, v. 103, No. 47, 2356–60, 5 fi [13 refs.] English summary.

An investigation into the pathogenesis of byssino has been carried out on 2 persons who had not pre ously been exposed to cotton dust. 3 gm. of cotton w rubbed with 50 c.c. of saline and allowed to stand at 4 for 12 hours, the liquid was then removed by filtrati

and administered by aerosol, causing prolonged dyspnoea and general malaise. The changes occurring in the lungs were studied by following the rate of washing out of nitrogen on breathing pure oxygen, which was determined by means of an automatic gas analysis apparatus which continuously recorded the nitrogen content of the expired air. The results were expressed as the lung clearance index; normal persons gave a value of 6–10 litres, indicating that 6–10 litres of air were ventilated per litre of lung volume during the process of reducing the nitrogen content of the expired air to 2%. In the first experimental subject the index rose from 8·3 to 10·2 after inhalation of the cotton extract, and in a repetition of the test carried out 2 months later some increase in sensitivity was observed, the index rising from 7·2 to 11·0. The second subject, who suffered from asthma, was much more sensitive to cotton extract, the index rising from 9·1 to 21·1 after inhalation. The reduction in ventilation caused by the extract was reversible, and passed off after a few hours. When a second inhalation was given 1 day after the first no effect was observed. It is concluded that cotton extract contains a substance, probably a releaser of histamine, which produces bronchial constriction and gives rise to a period of insensitivity.

D. J. Bauer

Cancella, L. de C. Suberose. Alterações pulmonares relacionadas com a inalação de poeiras de cortiça. **[Suberosis. Pulmonary Changes Associated with Inhalation of Cork Dust]** [Thesis.] 283 pp., numerous illustrations. [Numerous refs.] English summary. Parede: Casa N.S. da Bonança, Av. Marginal, Portugal.

Portugal is the most important cork producing country in the world, with about 980 cork mills employing 20,500 workers. The author has had the concept of suberosis, an occupational lung disease due to cork dust (from *Quercus Suber L.* the cork oak) since 1949, having been struck by the number of cases of chronic non-tuberculous chest disease occurring in workers in the cork mills.

This thesis is a record of the author's investigations. Of its 283 pages 18 are devoted to references to publications on chest disease. In addition there are summaries in French, German and English, each of 19 or 20 pages. There are several tables and 171 illustrations. The English summary which is reviewed here, has been carefully compiled, each paragraph dealing with the subject matter of a particular chapter of the Portuguese text, with numerous references to tables and illustrations so that these may be examined.

Analyses of the cork samples collected from the factories showed amounts of free silica from 0·9 to 3·1% comprising between 19·5 and 26·5% of the ash. Most of the silica was present in the bark and *nail* [*nail* is written in italics. The reviewer has been told it is not a botanical term. The corresponding Portuguese word in the text would appear to be costas which is used in inverted commas— "*costas*" (fig. 2).]

Animal experiments with 110 guineapigs and 32 rabbits included inhalation exposures, and intraperitoneal, intramuscular, subcutaneous and intravenous injections. These showed that cork is not inert. Generally an inflammatory reaction is provoked leading to ultimate fibrosis but without complete cicatrization. Inhalation for over a year produced focal lesions which are described as pneumoconiotic. The changes are shown in many well reproduced photomicrographs. In the guineapigs 3 incidental diseases occurred—a parasitosis, a storage disease probably of proteins, and a haemosiderosis.

In man, symptoms of nasal irritation, generally insignificant but occasionally more pronounced, were seen during the first 3 weeks of employment. After about 5 years there appeared cough, sputum, frequently blood-stained, chest pains, and decrease in working capacity. In some cases exertional dyspnoea appeared early. There were also variable digestive disturbances. Chest examination sometimes revealed an emphysematous configuration, with other signs of emphysema and bronchitis. Cyanosis was rarely found. The most significant of the laboratory investigations is stated to be the failure to demonstrate tubercle bacilli in the sputum. Blood sedimentation rate was slightly elevated but the blood was otherwise normal, there being no eosinophilia in 3,143 examinations of cork workers, in spite of the prevalence of eosinophils in many bronchial biopsy specimens.

Bronchoscopies revealed only a non-specific diffuse bronchitis, and bronchial biopsies an infiltration of the mucosa by inflammatory exudate cells. The proportions of different cells varied, eosinophils as stated sometimes being high. Necrotic cells and nuclei were usually present, also macrophages containing dust particles. In some preparations there were fibroblasts and new capillary formations. A search for fungi was negative and cutaneous tests for sensitivity to fungi and to 5 different types of cork dust in suberotic patients including two with asthma, were negative with the exception of one person positive (+) to cork.

Pulmonary function tests were done on 26 patients, and usually showed a high residual volume, and lowered vital capacity, maximum breathing capacity, and lowered oxygen minute volume. The pulmonary ventilation insufficiency was in some cases of serious degree, and it seemed that the parenchymatous involvement (fibrosis and emphysema) exceeded in importance the bronchial (spasm and obstruction).

A large number of chest radiographs are excellently reproduced. The various abnormalities which these show (reviewer's interpretation) include increased lung markings, increase in size and density of hilar regions, reticulation and honeycombing, nodular opacities, sometimes large soft parenchymal lesions and increased translucency. The nodular opacities are soft and often streaky and not very suggestive of pneumoconiosis. 9 macroradiographs are included which show the lesions enlarged and in higher contrast. Tomography helped in the visualization of changes in the parenchyma *e.g.*, emphysematous bullae, and in the bronchial, vascular and hilar patterns but did not give diagnostic evidence of conclusive value. Angiopneumography (14 patients) showed retardation of venous circulation and various abnormalities of position and size of vessels, and bronchography (6 patients) also showed irregularities of position and calibre of bronchi, including bronchiectasis. The author used his own radiological classification, which is very like that

suggested by the ILO Meeting of Experts, Geneva, 1958 [see this *Bulletin*, 1960, v. 35, 21] but neither in the summary, nor, it would appear, in the text, does he give the total number of cases examined by X-ray or the numbers in the different X-ray categories.

Material for studying morbid anatomy was obtained from 3 autopsies, 1 lobectomy and 1 biopsy. Dust-filled macrophages occurred singly and in clusters, and especially in sub-pleural zones, groups of cell-filled alveoli formed conspicuous but poorly delineated foci. Alveolar walls were thickened, mainly by cellular infiltration but also by fibres. Sometimes fibrosis was a marked feature (this is not specifically illustrated but some of the focal infiltrations were large). There were also infiltrations round the vessels, in the bronchial mucosa and in the interlobar septa. The tracheo-bronchial glands contained many dust cells, and sometimes the normal structure was replaced by capillaries, pre-collagenous fibres and eosinophils. It is stated that all the foregoing cellular and fibrous changes could have been caused by the free silica in the cork rather than by the vegetable particles.

After differential diagnosis, complications are discussed, bronchitis being stated to be frequent, lung cancer almost non-existent (1 case in 5,000 employees, and he had no contact with cork) and spontaneous pneumothorax being found in 7 out of 121 suberotic patients (5·8%). Tuberculosis creates difficulties in diagnosis and there is a high incidence in cork workers. The author's work on its possible relationship with suberosis has not so far been conclusive and is continuing.

There is no special treatment for suberosis. Prevention depends on dust suppression, and pre-employment and periodic medical examinations are recommended.

[This is an excellent work which gives the impression of having been carried out with care. Actual environmental conditions do not appear to be fully described, nor dust counts given, but the author makes out a convincing case for the existence of a chronic occupational lung condition due to cork. He tends to liken it to silicosis, and there are points of similarity, but it seems to the reviewer that the disease has more the character of a bronchitis, due to irritative or inflammatory changes—symptomatology (early cough and sputum rather than dyspnoea), radiological appearances and pathology all apparently favouring this. It is to be hoped that studies of this condition will continue, with examination of further autopsy material by large lung sections and other methods, including analyses of lung dust.]

[For previous studies, see this *Bulletin*, 1957, v. 32, 969.] *A. T. Doig*

DOMINICI, L. M., MICHELONI, F. & BIGOTTO, M. R. Le intossicazioni da piombo nell'industria ceramica della Repubblica di San Marino. [**Lead Poisoning in the Ceramic Industry of San Marino**] *Igiene e San. Pubblica.* Rome. 1960, Jan.–Feb., v. 16, Nos. 1/2, 13–22. [13 refs.] English summary (7 lines).

The Republic of San Marino has a long history of work with ceramics, chiefly glass, but cases of lead poisoning have only rarely been reported though 300 persons out of a total population of the republic of 15,000 are employed in such work. 2 large establishmen employ 145 and 85 persons respectively the remaind working in small workshops where the hygienic conc tions leave a good deal to be desired.

In the manufacture of the so-called " lead glass " Pb and red lead are used in considerable amounts as flux to make the colours adhere to the matrix and to mal them more brilliant, the amounts of PbO varying from to even 40%. The authors examined all 300 worke clinically and selected basophilia as the simplest ind of early Pb absorption and though not even those longe in the industry showed evidence of overt Pb poisonin in some the history of digestive disturbances etc. w suggestive. However 30% showed evidence of E " impregnation " which was not necessarily related to ag sex, type, or length of work, suggesting some continge condition which the authors consider was essential neglect of the rules laid down, particularly referen being made to the neglect of personal cleanliness, espec ally of the hands, as a potent accessory factor.

Nevertheless 30 persons, 14 male and 16 female, we found to have a basophil rate of 1:300. Their ag ranged from 12 to 67 years (only 2 were over 40 yea and the length of time they were exposed to risk vari from 25 days to 50 years though only 4 had done su work for more than 10 years. The authors consid that regular medical inspections at brief intervals togeth with the examination of blood films for basophilia essential for prevention together with education of t operatives as to the possible risk.

[6 of the 30 with high basophilia had done such wo for a maximum of 8 months, and only 1 of these w over 20. It might well be thought that when a child 12 who had worked in the decorating section for *on 25 days* had so high a degree of basophilia, the ris were considerable.] *W. K. Dunscombe*

STREIT-PAWLOWSKA, I. & SENCZUK, W. Zagadnien ołowicy w wybranych działach stoczni. [**Lea Poisoning in Some Dock Departments**] *Me Pracy.* 1960, v. 11, No. 2, 109–16. [15 refs.]

The English summary appended to the paper is follows:—

" The determination of lead level in the urine of 2 dock workers was performed. Among them 122 painte and 67 cabling workers were exposed to lead. 11 worke employed as administrative staff represented the contr group. In 72 persons from the group exposed to lead t lead level in urine exceeded 120μg/1. Calcium Disodi Versenate (CaNa EDTA), vitamin B_{12}, vitamin H vitamin C, liver extract ('Hepafort') and ferrugino preparations were administered orally during 14 days these persons. At the end of treatment the determinati of the lead level in urine was repeated. It was stated th in the group of persons in which before treatment t average lead level in urine amounted to 211 μg/1, af the therapy it decreased to 70 μg/1. The similar resu were obtained in the group in which before the thera the average lead level in urine was 145μg/1 and after 83 μg/1.

The authors conclude that in the lead poisoning pr phylaxis, besides the technical prophylactic measur

he improvements in plant sanitation and hygiene are of reat importance. Moreover, the authors stated that eriodical lead level determinations in urine are impor-nt for the early lead poisoning diagnosis."

ETTINATI, L., RASETTI, L. & RUBINO, G. Intossicazione da naftenato di piombo contenuto negli olii lubrificanti per sistemi idropneumatici. [**Poisoning by Lead Naphthenate present in the Lubricant Oils for Hydropneumatic Systems**] *Rass. Med. Indust.* Turin. 1959, Sept.–Oct., v. 28, No. 5, 379–85, 1 fig. English summary (9 lines).

The authors describe the case of a workman who had een complaining of digestive troubles for some 2 years: neither of the 2 hospitals which he had already tended had a diagnosis been made. A more careful vestigation of the history had now raised suspicion f lead poisoning and the subsequent examinations of lood, urine, etc., had confirmed this. The patient had een employed on the testing of hydraulic hoists installed y garage firms to help them in the maintenance of motor ehicles.

The authors then investigated 3 other men who llowed the same occupation as the first, and they found vidence of lead adsorption in 2 of these. In the case hich proved negative the man had been doing this ork for only 7 months whereas the exposure of the ther 3 to the lead hazard had lasted from 5 to 12 years.

The design and mechanism of the hoist is described in is paper and the oil used in its hydraulic action and ubrication was shown to contain 260 mgm.% of lead, hich is derived from the lead naphthanate which is ixed with the oil as a "mild EP additive."

The picture of lead adsorption or poisoning in these ases was characterized by a synovitis of the knee-joint. he authors suggest that the metal is absorbed by the kin and that the mineral oil helps this by giving rise to ritation and dermatitis. *J. Cauchi*

AOLETTI, G. Contributo allo studio della diagnosi precoce del saturnismo professionale. [**A Contribution to the Study of Early Diagnosis of Occupational Saturnism**] *Rass. Med. Indust.* Turin. 1959, Sept.–Oct., v. 28, No. 5, 386–99. [15 refs.] English summary (7 lines).

This paper first deals with occupational lead poisoning n general terms, touching on the history of this condition vhich has been recognized and described since very ncient times. The author then outlines the circumstances f the lead hazard as it affects workers in potteries when hey are handling insufficiently baked china and when and-painting or colour-spraying the articles.

He describes the cases of 3 of these women workers vhom they have recently treated for lead poisoning, and ompare the older investigation techniques, which esti-nated the lead content of blood and urine and looked or basophilia, with more recent methods, which study he exchange of porphyrin in the blood and the urine. He considers that an increase in the protoporphyrin content of the red cells is an early, constant and specific sign of occupational lead poisoning. *J. Cauchi*

PEDINELLI, M. & STRINGARI, M. Osservazioni sul trattamento "per os" con chelanti in lavoratori addetti alla produzione del piombo tetraetile. [**Oral Treatment with Chelating Agents of Operatives producing Tetraethyl Lead**] *Rass. Med. Indust.* Rome. 1959, Nov.–Dec., v. 28, No. 6, 514–25, 11 charts. [10 refs.] English summary.

The authors point out that Ca EDTA given intravenously is less effective in chelating organic than inorganic Pb so, in order to try and avoid the disadvantages of intravenous dosage, they have tried the effect of giving oral doses of versenate in a factory making tetraethyl lead where the operatives were exposed more or less permanently to a possible source of Pb poisoning. They mention that in some phases of tetraethyl lead manufacture the operatives are exposed to the risk of tetraethyl lead *per se*, and in others there is a risk of poisoning by Pb itself, hence the necessity for using treatment which will deal with both the organic and inorganic Pb. However, thanks to the factory's careful preventive measures no true case of Pb poisoning has occurred so consequently the amounts of Pb circulating in the bodies of the operatives must be small.

11 men who were found to have Pb amounting to 200 μgm./litre urine were at once transferred from the sections where they were at risk to other departments and were given prophylactic oral treatment with tablets of versenate or of cysteamine tartrate (beta-mercaptoethylamine). Treatment was given in cycles of 8–12 consecutive days (subsequently repeated) in doses of 1–1·5 gm. = 4–6 × 0·25 gm. tablets of versenate, or tablets of 0·2 gm. cysteamine tartrate. 9 patients were given the versenate, 1 combined versenate and cysteamine tartrate, and 1 cysteamine tablets only.

Treatment was very well tolerated by all the patients but the multiplication effect on urinary excretion was much less than when EDTA is given intravenously while there seemed to be a lesser effect on organic than inorganic Pb. The action of the beta-mercaptoethylamine was slower and rather less than that of the EDTA tablets. *W. K. Dunscombe*

OLLINO, P. & BREUSA, M. La funzionalità tiroidea nel mercurialismo cronico. [**The Thyroid Function in Chronic Mercury Poisoning**] *Rass. Med. Indust.* Turin. 1959, Sept.–Oct., v. 28, No. 5, 331–60, 14 figs. [Numerous refs.] English summary.

The authors have studied the functioning of the thyroid gland in 11 subjects, 10 of them women, whose ages ranged from 44 to 68 years and who had a history of chronic mercury poisoning which had lasted between 11 and 15 years. All were native of the same province and had lived in the same town for at least 40 years, and their cases were eminently comparable.

After administration of sodium iodide, radionucleide ^{131}I given by mouth in the equivalent dose of 120 micro-Curies (the women were well past the menopause), the

authors plotted the thyroid uptake of radioactive ^{131}I and, using an X-ray scanning technique which they describe, they studied the distribution of the isotope in the various segments of the gland. They reproduce pictures of the isotopograms which they obtained.

The authors also determined the amount of iodine taken up in the plasma protein and they measured the basal metabolic rate.

The findings in this investigation indicated increased thyroid activity in 7 out of the 11 subjects and the authors believe this hyperactivity to be a clinical manifestation of mercury poisoning and to be due to the action of the metal on the regulatory centres in the hypophysis and other parts of the diencephalon. *J. Cauchi*

WILLIAMSON, W. H. & CLAY, M. F. **Treatment of Exhaust Gases from Boron Fuels.** *Amer. Indust. Hyg. Ass. J.* 1960, Apr., v. 21, No. 2, 110–14, 6 figs.

(i) LIEBEN, J. & METZNER, F. **Epidemiological Findings associated with Beryllium Extraction.** *Amer. Indust. Hyg. Ass. J.* 1959, Dec., v. 20, No. 6, 494–9, 2 figs. [17 refs.]

(ii) WATTS, S. R., WALSH, F. X. & VOUGHT, Virginia M. **Analytical Experiences with Beryllium Determinations in a Comprehensive Air Pollution Study.** *Ibid.*, 500–503, 2 figs.

(iii) SUSSMAN, V. H., LIEBEN, J. & CLELAND, J. G. **An Air Pollution Study of a Community surrounding a Beryllium Plant.** *Ibid.*, 504–8, 4 figs. [11 refs.]

In 1937, a beryllium extraction and metal fabricating plant started operations close to a rather densely populated area in Pennsylvania. For many years it has been known by some, though denied by others, that this plant has caused cases of beryllium disease. These papers give the preliminary findings of a study started in 1957 by the Division of Occupational Health of the Pennsylvania Department of Health.

58 cases of chronic beryllium disease are described: 26 of them were fatal. Approximately one-third of the cases occurred among those who worked in the plant, another third among those who handled contaminated work clothes of plant workers and the rest among those who lived, or frequently visited, in the neighbourhood of the plant.

The pollution of the air with beryllium in the neighbourhood of the plant was measured. Details of sampling and analytical techniques are given.

"The air sampling program was not conducted during the actual time when air pollution is believed to have caused the neighborhood cases, but it can be conservatively assumed that similar or higher concentrations would have been found in the past."

Despite this, the mean concentration of beryllium was still found to exceed the tentative maximum atmospheric concentration, recommended by the Atomic Energy Commission. The authors conclude that:—

"The data contained in this preliminary report sufficient to require that additional controls be emplo by the plant so as to reduce atmospheric concentrati of beryllium in the vicinity of the plant."

C. H. Woo

MINISTRY OF LABOUR. H.M. FACTORY INSPECTORA **Toxic Substances in Factory Atmosphe** *Safety, Health & Welfare, n.s. No. 8.* 12 pp. 1 Mar. London: H.M. Stationery Office. [1s.]

The Factories Act, 1937, requires that all practica measures shall be taken to protect persons emplo against inhalation of any dust, fume or other impu of such a character and to such an extent that it is li to be injurious. This booklet offers suggestions to t concerned. It deals with measures to protect aga inhalation and gives information about certain dusts fumes.

In some instances the hazards and the proper p cautions are well understood, but with the developm of industrial processes new substances are coming use. It is of prime importance to be on the look- for a possible hazard and to bear in mind the poss need for precautions. Labels on containers, and inst tions for the use of materials, should be prop examined, understood and observed.

Obviously, the best method of preventing exposur toxic material is to use harmless substances. If it is possible to substitute a harmless substance it may stil possible to use a less harmful one.

If substitution is impossible and a toxic material m be used, the next best protection is to ensure that injurious material can escape into the air of the wo room. This can be ensured by total enclosure of plant—preferably with the enclosed plant at a slig reduced pressure. Devices analogous to total enclo include the use of wet methods where dust is contai by liquid.

If both substitution and total enclosure are impra cable the next best way is to apply the principle of fume cupboard as used in chemical laboratories.

When the foregoing methods cannot be applied question of local exhaust arises, but this method is efficient than any of those already mentioned. Local haust should be designed to enclose the source of c tamination as far as possible, and the air speed at point of origin of the dust or fume must be high eno to ensure that the dangerous material is drawn a from the worker.

There are a very few instances where toxic materia generated and cannot be adequately controlled by an these methods. Then appropriate respirators or o breathing apparatus should be provided and worn. S toxic materials can be absorbed through the skin, workers exposed to these materials should wear pro tive clothing.

Some guide to the efficiency of measures of contr desirable. At the end of the booklet 6 pages are dev to a comprehensive list of maximum permissible con trations in the atmosphere of gases, vapours, and t dusts, fumes and mists. The concentrations given

based on those formulated by a Committee of the American Conference of Governmental Industrial Hygienists, and they relate to average concentrations for a normal working day. *Thomas Bedford*

GRANDJEAN, Etienne. Die arbeitshygienische Bedeutung von Tri- und Perchloräthylen. **[The Industrial-Hygienic Importance of Trichloroethylene and Perchloroethylene]** Reprinted from *Indust. Organisation.* 1959, No. 7, 14 pp., 10 figs. (2 on 2 pls.) [12 refs.]

Trichloroethylene (Tri) and perchloroethylene (Per) have similar solvent properties but Tri has a lower BP (86·9°C.) than Per (120·8°C.), a higher vapour pressure and is somewhat more volatile. The atmospheric concentration in the workroom will therefore have a higher level of Tri.

When either comes in contact with flame or hot metal, phosgene, carbon monoxide and hydrochloric acid are liberated; Tri is also decomposed at temperatures above 120°C. or by contact with aluminium chloride. Per is less readily decomposed and can be used for degreasing aluminium. Both are widely used in many branches of industry; both are used as degreasers in the heavy metal industry, but for light metals such as aluminium and magnesium Per is preferred; for large objects it can be used in vapour form.

In acute poisoning the mode of entry of both is by the lungs. On account of their solubility in lipids they pass readily through cell walls and membranes and have a special affinity for nerve cells which accounts for their powerful narcotic effect. They can be lethal if the concentration in the brain exceeds a certain threshold and if the respiratory and circulatory centres are affected.

For animals, the thresholds for narcosis and death are estimated as 3,700 to 5,000 p.p.m. and 7,400 to 27,000 p.p.m. respectively for Tri, and 3,000 to 9,000 and 5,000 to 12,000 p.p.m. respectively for Per. The onset of narcosis is slower with Tri.

For man, the thresholds for Per are 50 p.p.m. for perception by smell, 500 for slight malaise after 2 hours, 1,000 for slight intoxication after 45 minutes, and 2,000 for light narcosis after a few minutes. For both Tri and Per the threshold of unconsciousness is between 1,000 and 2,000 p.p.m.

The most frequent cases of acute poisoning occur from the cleaning of large vessels which have contained Tri, its use in small unventilated spaces, accidental leaks from the apparatus and careless handling of large quantities. Concentrations arising from the cleaning of Tri baths by a flow of water or a hand brush have been estimated at 1,120, 815 and 395 p.p.m. 3 fatal cases are described where immediate removal to fresh air had not been carried out.

Chronic poisoning from both Tri and Per results from the retention in the tissues of their decomposition products, especially trichloroacetic acid, of which about 20% is excreted slowly in the urine.

The symptoms of repeated exposure to Tri vary with individual susceptibility. The author has investigated 73 workers in the Swiss machine industry and has collected examples from the literature.

Liver injury is rare and occurs only in predisposed individuals. Blood changes, though anaemia is more common in Tri workers than others, are attributed more to unsuitable diet and hygiene than to Tri. Digestive disturbance, especially loss of appetite, occurred in 28% of the workers investigated, and 20% were underweight. Upper respiratory irritation in the form of catarrh was a feature of exposure to both solvents, but severe lung affection is only to be expected from massive exposure or inhalation of decomposition products.

Subjective nervous disorders—giddiness, lassitude, headache, irritability, insomnia and drowsiness—and objective signs—tremor of the fingers, disturbances of gait and eye movements, skin sensitivity and altered reflexes—were present in 28% of the author's cases; other observers have reported paralysis of the trigeminal and optic nerve and polyneuritis. Disorders of the vegetative system—excessive perspiration, coldness of the hands, functional gastro-intestinal disturbance, rapid pulse, extra systoles and cardiac pain were present in 36%.

Organic psychic disorders of thought, memory, concentration, mental agility and imagination were not specific but were regarded as a result of mechanical injury of the brain similar to that of alcoholism or arteriosclerosis. These disorders have been classified in 3 phases; first, slight disturbance of psychic function provoked by alcohol, to which 30% of cases showed intolerance; second, manifest disturbance of memory, attention, mental quickness and affectivity; third, symptoms of paralysis. The first and second phases are curable after a year's cessation of exposure to both Tri and Per. Among the 34% of cases so affected, half were also alcoholics or arteriosclerotics.

Skin injuries by Tri were chiefly eczema, either acute and superficial, or allergic, leading to sensitivity to other substances and localized to the hands and forearms.

Per injuries have been less frequently reported owing to its lower volatility, but materials soaked in it take longer to dry.

Control of atmospheric concentrations can only be achieved by estimation of their level, either by a hand pump, which gives readings inaccurate from 10 to 20%, or by a colorimetric method, with air pumps placed at various levels. In a few work places in a machine shop the level reached 335 p.p.m. The highest average values (59·5 and 53·8 p.p.m.) were found with open apparatus but values were nearly as high with closed; they varied considerably with the time of day. Among 50 workers examined nervous disorders were more frequent in those exposed to more than 40 p.p.m. and for a longer time.

The recommended MAC varies from 200 p.p.m. in the U.S.A. to 30 in Scandinavia and 9 in Russia. The author recommends 40 p.p.m. and states that with careful handling and suitable apparatus the MAC can easily be kept to 20 p.p.m. or less. Illustrations of apparatus for cleaning metal parts and clothing and a diagrammatic scheme for an automatic degreaser demonstrate how the concentrations can be kept to a minimum. In Switzerland, rooms with cleaning apparatus must have a capacity of at least 50 cubic metres, or more if the apparatus contains more than 100 litres of Tri or Per.

All containers should carry warning labels; Tri should not be heated above 120°C. and Per above 150°C.

Contact with open flame or red-hot materials should be prevented and the materials to be cleaned should be free from acids or alkalis. Careful handling of soaked clothing is essential, with sufficient time for drying in the neighbourhood of the exhaust ventilation or in a special automatic drier for small articles.

Exhaust ventilation with provision for entry of fresh air is necessary for both open and closed apparatus.

Other recommendations include instruction and explanation to the workers of the potential hazards of Tri and Per; personal cleanliness; respiratory masks for special conditions, with an activated carbon filter for concentrations of 200 to 1,000 p.p.m. for not more than half an hour, and with fresh air inlet for work in closed tanks; prohibition of the practice of one person working alone in high concentrations; gloves of polyethylene with a soft lining to absorb perspiration, or of leather if the hands have to be immersed.

The main value of barrier creams is their facilitation of thorough cleansing of the hands; mild soaps only should be used, and adequate washing facilities will reduce the incidence of eczema.

Persons with neurological disorders or with a tendency to alcoholism, liver disturbance or eczema should be excluded, and medical examinations should be carried out annually. *Ethel Browning*

LEVADIE, B. & HARWOOD, J. F. **An Application of Gas Chromatography to Analysis of Solvent Vapors in Industrial Air.** *Amer. Indust. Hyg. Ass. J.* 1960, Feb., v. 21, No. 1, 20–24, 5 figs.

In the 2 techniques described, meta-xylene was used as the scrubbing or trapping solvent because its boiling point and chromatographic retention time are satisfactory for environmental studies in industry, particularly for the low boiling point organic solvents. Chromatograms illustrate the clear-cut results obtained, and the traces of impurities, present in even spectrographic grade meta-xylene, do not confuse the tracings.

In selecting components of the apparatus and in assessing optimum rates of flow, methylene chloride was the substance tested because of its high vapour pressure: a high rate of scrubbing efficiency would assure reasonable recovery of substances with lower pressures. In the 1st method, 0·1 cu. foot of air to be tested is scrubbed through 2 midget impingers in series, each containing 10 ml. meta-xylene, at a sampling rate of 0·0133 cu. foot per minute; the impinger contents are pooled and 0·05 ml. chromatographed. The other method of sampling was designed to increase the sensitivity of the test by using a modified Australian bubbler. This has the advantage of needing only 1 scrubber and 5 ml. meta-xylene. High recovery of low traces of atmospheric contaminants was possible when 0·15 cu. foot was passed at 200 ml. per minute.

Chromatograms reproduced include one of a mixture of 100 p.p.m. each of tetrachloroethylene, trichloroethylene, carbon tetrachloride and dichloroethylene, another of 100 p.p.m. of toluene and benzene and another of solvents containing benzene. Mean retention times and peak heights are shown in tables from data obtaine from typical chromatograms of air samples containin methylene chloride, carbon tetrachloride, trichloroeth lene and perchloroethylene at concentrations of 100 ar 200 p.p.m. A quantitative analysis of a mixture of chlo nated hydrocarbons gives typical recoveries by th method. *M. Patricia Fitzsimons*

HAUSMAN, A. Les méthodes modernes d'analyse rapic du CO dans l'atmosphère. [**Modern Methods fo the Rapid Analysis of Atmospheric Carbo Monoxide**] *Arch. Belges Méd. Sociale, Hyg., Mé du Travail et Méd. Légale.* 1960, Mar., v. 18, N 3, 188–200, 5 figs. (1 folding).

HILL, W. H. & MERRILL, Jean M. **Determination Pentaborane in Air by means of Activate Carbon.** *Amer. Indust. Hyg. Ass. J.* 1960, Feb v. 21, No. 1, 15–19. [12 refs.]

This preliminary report describes relatively simp apparatus for exposure chamber monitoring. Difficulti and variables encountered during inhalation studies a discussed and tests for boranes reviewed. Pentaboran behaves differently from diborane and decaborane, b activated carbon adsorption had been found useful respirator development work. The method is now givi good results at concentrations of 0·2 p.p.m. in other wo which is to be published. Meanwhile work is also bei completed on a triphenyltetrazolium chloride method.

The collection equipment, made practically all of gla is an upright tube with a fritted plate fused inside an ball and socket joints for the connexions. It contai 5 gm. activated carbon of specially low boron conten For pentaborane concentrations of 0·2 p.p.m., the s sample was 50–100 litres and for 15 p.p.m., 1–3 litre sampling rates varying from 0·2 to several litres p minute. Methods for determining the boron adsorbed the carbon proved difficult. Tables give results aft methyl borate distillation which was preceded by toluen or benzene azeotropic distillation or by treatment wi NaOH.

Nominal inlet concentrations fluctuated. Some pent borane was hydrolysed or oxidized during circuit an some may have been absorbed by the chamber varni and animals' fur. Nevertheless, results show figur which represented prevailing concentrations with fair r liability, and tubes tested in series showed almost com plete retention in the first. Cylinders of the pentaboran nitrogen mixture were tested and analysis showed th oxygen was important for carbon adsorption; progr sively lower concentrations were found as the amount gas passed through the sample tube was increased.

The method is not specific, but diborane and dec borane, if present in the atmosphere, can be estimat separately. Moreover, the toxicity of the various boran is of the same order of magnitude, and summation the atmospheric concentrations would not detract fro the value of the result. *M. Patricia Fitzsimons*

DANZIGER, H. **Accidental Poisoning by Vinyl Chloride: Report of Two Cases.** *Canadian Med. Ass. J.* 1960, Apr. 16, v. 82, No. 16, 828–30. [12 refs.]

2 similar rapidly fatal cases, the second proved by circumstances to have been caused by vinyl chloride, illustrate dangers when safety rules are disregarded and toxicological difficulties of proof of poisoning from volatile gases. Also called chloroethylene or chloroethene, $CH_2 = CH.Cl$ is an explosive, heavy and volatile gas; BP −14°C. In enclosed production of polyvinyl resin, polymerization is not completed and, before a tank is opened, residual vinyl chloride is pumped into another recovery tank. The residual gas contains 90% vinyl chloride, 8·5% CO_2, vinyl acetate, trichloroethylene, N and argon.

The first patient entered a tank to clean it, after the usual safety tests. Air was continuously exhausted and replaced, but the air hose afterwards appeared defective. He did not wear the required safety belt and line. Nor was the required rescue apparatus immediately available when, 10 minutes later, he failed to answer. The rescuer could not detect vinyl chloride. The second patient was found beside an open valve 20 minutes after he had entered a pit outside the recovery tank to open this water outlet valve from this tank. One rescuer closed the valve, was affected by escaping gas, became giddy, saw circles, crawled away shouting and recovered quickly; another, wearing a respirator, removed the body. Both of the men who died had often done these tasks.

At autopsy, performed 3 and 8 hours later, no vinyl chloride was found. It may have been expelled by artificial respiration. The pathological findings in both were cyanosis, conjunctival burns, congestion of internal organs, especially lungs and kidneys, and failure of the blood to clot. Though not diagnostic, these findings were observed in experiments with vinyl chloride and are being published. The first patient, aged 21, also showed slight heart and kidney disease. He may have fainted before being asphyxiated. Vinyl chloride rapidly induces narcosis and, in dogs, causes cardiac abnormality. It is considered one of the least dangerous of chlorinated hydrocarbons; the MAC is 500 p.p.m.

M. Patricia Fitzsimons

PETTINATI, L., SCANSETTI, G., CAPELLARO, F., GAIDO, P. C. & RASETTI, L. Indagini sull'esposizione cronica al meta-amino-fenolo e para-nitro-etilbenzolo. [**Investigations on Chronic Exposure to Meta-Amino-Phenol and Para-Nitro-Ethyl-Benzol**] *Rass. Med. Indust.* Rome. 1959, Nov.–Dec., v. 28, No. 6, 437–46. [18 refs.] English summary.

The authors examined 18 persons, 12 of whom were exposed occupationally to risk of poisoning by meta-aminophenol, and 6 by paranitroethylbenzol, whose ages ranged from 24 to 51, and the length of time at such work from 2 to 7 years. All the patients showed definite clinical signs, with cyanosis especially of the lips a prominent symptom and almost all had hypotension when examined at the end of the shift; in 9 patients when examined after 1 day's holiday, *i.e.*, about 32 hours after ending the shift there was no material difference from the original findings. The patients mostly complained of asthenia often accompanied by headache (in both groups) and 2 showed grave and 4 marked cyanosis. Methaemoglobin levels did not differ much in the 2 kinds of risk and 1 day's holiday was sufficient to reduce the MetHb level to nearly normal but in 3 patients even though this was within normal limits, cyanosis was unchanged even after 1 week's absence.

The authors discuss carefully this persistence of cyanosis with normal MetHb levels and suggest that it is due to slowing down of the peripheral circulation due to the diminished oxygenation of the blood. The free erythrocytic and the urinary coproporphyrin behaved in the opposite manner, *i.e.*, they rose after absence from work. It thus appears that the toxic product causing the methaemoglobinaemia may also affect the enzyme systems synthesizing porphyrin.

W. K. Dunscombe

PALLADE, Sulamith, LONDON, Micaela, ROVENTA, Ana & POPOVICI, Carmen. La tossicità di un concime largamente usato in agricoltura: Il superfosfato. [**Toxicity of a Largely Used Agricultural Fertilizer: Superphosphate**] *Med. d. Lavoro.* 1960, Jan., v. 51, No. 1, 49–58, 5 figs. [25 refs.] English summary (8 lines).

This report comes from the section of Industrial Hygiene of the Institute of Hygiene and Public Health of Rumania. In it the authors point out that one of the very important components of superphosphate is fluorine which sometimes during manufacture has led to severe symptoms of mottled teeth, digestive disturbances, bony changes, atrophic rhinitis, and ulceration of the nasal mucosa occasionally going on to perforation of the septum after prolonged contact. However the toxic action of the fertilizer is due not only to its F content but to the particular solubility of the F salts and to the physical state of the fertilizer. When given intragastrically to rabbits superphosphate is much more toxic than the apatite from which it is made; the urinary elimination of F gives a precise and convenient indication of the yield to F, but after administration of non-lethal doses to rabbits there was some retention of F. In these animals there appears to be some potentiating action of P on the F ions as regards toxicity and after 2 doses of superphosphate (90 mgm. F/kgm.) there was a marked reduction in the activity of the blood phosphatase but not in cholinesterase though *in vitro* this was also reduced.

The authors conclude that in contrast to what has been thought hitherto superphosphate has a definite toxic action and repeated exposure of workers to small doses may have some effect. Hence the MAC should be established, bearing in mind not only the F content but also the complex composition of the product.

W. K. Dunscombe

SELTSER, R. & SARTWELL, P. E. **The Application of Cohort Analysis to the Study of Ionizing Radiation and Longevity in Physicians.** *Amer. J. Pub. Health.* 1959, Dec., v. 49, No. 12, 1610–20, 4 figs. [10 refs.]

One effect of exposure of laboratory animals to ionizing radiation is shortening of the average duration of life. One way of testing whether such an effect is produced by chronic exposure to small doses of radiation in man is to compare the longevity of radiologists with that of other specialists. In the present study the mortality of male doctors from the U.S.A. and Canada who became members of the American Roentgen Ray Society during the period 1905–54 is compared with the mortality of those who became members of the American Association of Pathologists and Bacteriologists. Differences between the groups in time of entry, age of entry and geographic location are small and unlikely to affect the comparison materially. The number of deaths among radiologists aged 50 years and over who entered the society between 1905 and 1914 (54) is higher than that which would have been expected at the mortality rates observed among the corresponding group of pathologists (42·1), but the difference is not statistically significant. In all other groups the differences are small and the total number of deaths among the radiologists (229) is only slightly higher than that expected (211·0). The mortality among radiologists was, moreover, similar to that of all U.S. doctors and somewhat lower than that of all U.S. white males.

Causes of death are not all known completely; but the present data reveal an excess mortality from leukaemia among the radiologists (standardized death rate of 69·3 per 100,000 men per year against 10·9) and an excess mortality from tuberculosis among the pathologists (standardized death rate of 36·1 per 100,000 men per year against 6·1).

The method of cohort analysis is a useful method for detecting differences in the hazards to radiologists practising at different periods, but larger numbers are needed to obtain definitive results. [For a previous study see this *Bulletin*, 1958, v. 33, 490.] *Richard Doll*

MCLAUGHLIN, J. E. **Nuclear Safety in Manufacturing Plants.** *Amer. Indust. Hyg. Ass. J.* 1960, Feb., v. 21, No. 1, 59–67, 6 figs. [12 refs.]

The author writes about safety measures in reactor fuel fabrications carried out in industrial plants not associated with the large Atomic Energy Commission plants. They operate either under government contract or the A.E.C. licensing programme. Assurance of nuclear safety is a three-stage problem. First, scientific considerations regarding nuclear properties with special reference to critical parameters. Second, engineering considerations of disposition of plant and third, administration of the requisite safety controls. The nuclear energy business has expanded so quickly that there are not enough people available to resolve the problems that arise during operations; especially when the undertaking is not on a very large scale. So independent analyses are conducted.

Design is constantly changing and the author refers *The Elements of Nuclear Reactor Theory* by GLASSTO and EDLUND (1952, New York: D. Van Nostrand Co A new technical term called "buckling" (B^2) is int duced, but the author refrains from giving its derivati and description as it is too technical. However o gathers that it is a measure of the curvature of t neutron flux as a function of position in a reactor co It is a geometric quantity, its value depending on t shape and size of the reactor. Its appearance in t literature will become more frequent as indeed the tabu matter in this article suggests which is highly techni throughout.

We are assured that nuclear safety should not depe on the occurrence of less than two unlikely events.

S. Rus

WELFORD, G. A., MORSE, R. S. & ALERCIO, J. **Urinary Uranium Levels in Non-Exposed In viduals.** *Amer. Indust. Hyg. Ass. J.* 1960, Fe v. 21, No. 1, 68–70, 1 fig.

Uranium is one of the potentially poisonous substan found normally in the body in extreme dilution. In dustrial processes using this chemical the chief risk health is in the inhalation of loaded dust and work are protected therefrom by a maximum permissible c centration, *viz*:—50 microgrammes per cubic me (EISENBUD and QUIGLEY, *Arch. Indust. Health*, Chica 1956, v. 14, 12), at which level they would excrete, by urine, about this amount per litre. Many industr workers show levels of 1–10 μgm. per litre.

The authors have examined the urine from 26 peo non-occupationally exposed to uranium. The met eventually reduces itself to a fluoroscopic method the sodium fluoride used in the fusion of material first to be got rid of as it completely masks uranium content of the sample. This is detailed in processes. Tests were carried out on 26 people on 5 whom they were continued for 10 weeks.

For the whole number sampled, the urine cont varied from 0·070 to 0·23 μgm. per litre. There was li variation among those submitting to the prolonged t

S. Rus

GOREN, S. & THORNTON, J. H., Jr. **The Inhalati Hazard from Dust-Producing Operations in t Repair of Ships with Low-Level Radioact Contamination.** *Amer. Indust. Hyg. Ass. J.* 19 Feb., v. 21, No. 1, 71–9, 6 figs.

The paper gives a good account of the radiat hazards met in the repair of a ship which had part pated in recent nuclear tests and showed moderate-le contamination.

Various processes are used to get rid of this conta nation and the hazardous operations are listed in or of their danger to the operative as follows: disc-sandi pneumatic wire-brushing, welding and pneum chipping.

As might be expected local ventilation in the immedi area of the dust-producing operation, exhausting the d and fumes from the operator are all important measu

safety. Mechanical filter type respirators appear tisfactory when dealing with surfaces showing an ctivity of 4 mrad/hour measured 1⅝ inches from the rface. The authors think that with greater surface ctivity it may become necessary to use masks with a ositive pressure flow of uncontaminated air or oxygen. The view is expressed that a need exists for better- ntrolled laboratory testing to obtain more accurate ata. The U.S.A. Naval Radiological Defence Labora- ry has work in hand on such projects. *S. Russ*

EVERETT, J. K. & BEASLEY, C. H. **An Investigation of Lens Opacity on Personnel Operating a Portable Nuclear Reactor.** *Amer. Indust. Hyg. Ass. J.* 1960, Feb., v. 21, No. 1, 84–6.

Ionizing radiation can induce cataract by degeneration the posterior cortical lens fibres in months or years ter exposure. The radiation cataract differs from other rms in that the cortex as a whole remains clear except r the small area in front of the posterior capsule. It is ated that 14 people in the U.S.A. have developed radia- on cataracts as a result of cyclotron-induced radiation posure.

The Convair-Fort Worth centre in Texas is one of the ajor contractors involved in nuclear propulsion for air- aft. The employees are exposed to nuclear radiation hich comes from 48 encapsuled polonium-beryllium sources ranging in strength from 1 to 50 curies and a radium source of 1 curie. In addition there are two nuclear reactors, a Ground Test Reactor and an Aircraft Shield Test Reactor, unique in the nuclear industry; they are portable and flexible in use. They can be operated deep in water or high in air.

Although there is strict medical supervision of the whole personnel, the present account refers in detail only to the findings of the slit-lens eye examinations of all employees exposed to neutron radiation. Over 4½ years 655 examinations have been made. Lens opacities were found in 24 of the examinations carried out; 15 of these were of the congenital variety and 9 were developmental.

Details are given of the clinical findings. *S. Russ*

ABEE, H. H. & COTTRELL, W. D. **Contamination resulting from the Release of Radioactive Liquid Wastes to the Tennessee River System.** *Amer. Indust. Hyg. Ass. J.* 1960, Apr., v. 21, No. 2, 156–61, 7 figs.

MARTIN, J. H. **Radiation Biology. Proceedings of the Second Australasian Conference on Radiation Biology held at the University, Melbourne, 15–18 December, 1958, by the** AUSTRALIAN RADIATION SOCIETY.

This book was reviewed on p. 526.

Food and Nutrition

The order in this section is:—**General; Foodstuffs; Food Poisoning.**

FOODSTUFFS

Composition and Bacteriological Control

IUDEMANN, H. Zur Bedeutung von Typhus-Vi- und *Salmonella*-Phagen in Lebensmitteln. [**The Significance of Typhoid Vi and Salmonella phages in Foodstuffs**] *Arch. f. Hyg. u. Bakt.* 1959, Nov., v. 143, No. 7, 495–500. [13 refs.]

61 samples of foodstuffs of animal origin and 79 amples of vegetable origin obtained from retail stocks n Germany were examined for contamination with yphoid Vi and other *Salmonella* phages. The samples vere minced and extracted with sterile saline; determina- ions were made of the *Escherichia coli* titre and the con- ent of *Salmonella* spp. and total organisms in the ex- racts, and phage was detected in filtrates or heated xtracts by enrichment with an indicator organism. Vi- hage was found in 13 and *Salmonella* phages in 5 amples of vegetable foodstuffs, and with foodstuffs of nimal origin the corresponding figures were 7 and 37 espectively. No *Salmonella* spp. could be isolated from ny of the samples, and no definite relationship could be observed between the presence of phage and the *E. coli* titre or total content of organisms. The presence of Vi phage in foodstuffs is regarded as an indication of the occurrence of faecal contamination of human origin.

D. J. Bauer

HOBBS, Betty, C. & WILSON, J. G. **Contamination of Wholesale Meat Supplies with Salmonellae and Heat-Resistant** *Clostridium welchii*. *Monthly Bull. Ministry of Health & Pub. Health Lab. Service (directed by Med. Res. Council).* 1959, Dec., v. 18, 198–206. [15 refs.]

For several years the Food Hygiene Laboratory (PHLS) at Colindale has been concerned with the possible dangers to health of imported foodstuffs which may be contaminated with salmonella and other pathogenic organisms. Dr. Hobbs has recently provided evidence, in conjunction with her colleagues at Colindale, to show

that certain egg products imported from overseas have have been responsible for many outbreaks in Great Britain of paratyphoid and other salmonella infections. The present report concerns an investigation, undertaken with the Medical Officer of Health of the Port and the City of London, into the degree of bacterial contamination of imported meat supplies, chiefly frozen blocks of boned-out veal, beef and mutton from different countries of origin. Carcass meat from comparable sources showed an overall salmonella contamination rate of 4·3%, against 10·3% for boned-out meat; the figures for clostridial contamination were of the same order. The contamination rate varied according to the country of origin and although the different groups are not strictly comparable there seems to be no doubt that of the specimens examined, boned-out veal was the most heavily contaminated with both salmonellae and *Cl. welchii*. Of some 300 samples taken from frozen blocks of boneless veal imported from the same country of origin salmonellae were isolated from 18% and *Cl. welchii* from 10·7%. The possible dangers to health of allowing such material to be placed on the retail market are obvious, since these frozen blocks average about 60 lb. each, and the retail disposal to local buyers will involve much handling and opportunity for cross infection of other meat products sold in the same shops; cross infection of the handlers themselves may also be considerable.

[The important observations disclosed in this report may have wide repercussions and detailed study is recommended.] *H. J. Bensted*

Tailyour, J. M. & Avery, R. J. **A Survey of Turkey Viscera for Salmonellae, British Columbia.** *Canadian J. Pub. Health.* 1960, Feb., v. 51, No. 2, 75–7.

"Viscera and intestinal content of 523 market weight turkeys were cultured for organisms belonging to the genus *Salmonella*. This represented 1% of the birds processed over a three week period in November and December, 1956, at one killing plant in Vancouver, B.C. under federal veterinary inspection. Four birds (0·76%) were found to be harbouring a *Salmonella* species identified as *Salmonella derby* (1, 4, 12; f, g—)."

Hughes, H. L. **An Investigation of the Bacteriological Condition of Cooked Meats as sold to the Public.** *Sanitarian.* London. 1960, Jan., v. 68, No. 4, 216–24.

282 samples of retail cooked meats were examined. They were collected after packing in the normal manner for a customer, then cut up with sterile utensils and transferred to a sterile jar; the age, origin and method of storage and display were noted.

94 (33%) were regarded as stale and unsatisfactory because of gross bacterial contamination; the highest proportion of unsatisfactory samples came from butchers' shops, owing, it was thought, to cross contamination from raw to cooked meat. Brawns and jellied veals were most susceptible to ageing and gave the worst results. It was recommended that these products should be sold within 5 days of manufacture on the premises, or within 3 days of delivery if manufactured elsewhere. One-third c of all samples were refrigerated in the shops; the that little difference was noted between the results of frigerated and non-refrigerated samples was thought be due to the age of the samples.

Examples of bacteriological results are given both satisfactory and unsatisfactory samples. Suggested st dards are based on colony counts at 37° and 20 (100,000 and 500,000 respectively), and absence of fae coliform bacilli and coagulase-positive staphylococci 1 gm., and of salmonellae in 25 gm.

A proposed Code of Practice for the handling cooked meat products during storage and sale is giv It is suggested that the bacteriological supervision of manufacture and retail sale of processed meats is one the newer fields of public health work, which sho receive increased attention by Public Health Inspect *Betty C. Hobb*

Worseck, M., Gürlich, J. & Hemlep, Ingebo Enterotoxische Staphylokokken in Rohmilch Berli Abmelkbetriebe. **[Enterotoxic Staphylococci Raw Milk Sold in Berlin]** *J. Hyg., Epidem Microbiol. & Immunol.* Prague. 1960, v. 4, No 123–30. [72 refs.]

The English summary appended to the paper is follows:—

"Cases of food poisoning due to enterotoxic stap lococci are described very frequently in other countr The authors submit a detailed index of the literature this problem, showing the importance of milk and da products as a source of infection.

"Since part of the milk consumed in Berlin at time the research was carried out was sold raw, it decided to carry out a microbiological investigation.

"Examination of 22 cowsheds produced 650 strains staphylococci, 16·7% of which were plasma-coagula positive. The majority also answered to known criteria pathogenicity. In an enterotoxic test seven strains w positive. After three years, phage typing resulted determination of group 42D in four of these strains. C strain died during this period and could not theref be tested, while the other two were plasma-coagula negative after two years. The possibility that the f strains were no longer the original strains is consider Random tests demonstrated that staphylococci occur raw milk in Berlin, but that certain factors of the lo environment appear to prevent food poisoning.

"From July 1, 1958, all raw milk sold in the dem cratic sector of Berlin is only scalded before being sol

Panes, J. J. & Thomas, S. B. **The Multiplication *coli-aerogenes* Bacteria in Milk stored at 3–** *J. Applied Bact.* 1959, Aug., v. 22, No. 2, 272 1 fig.

108 samples of raw morning milk from individ farm supplies were examined for *coli-aerogenes* or nisms on violet red bile agar, within 10 hours of p duction. After holding for 72 hours at 3–5°C. examination was repeated. 35·2% of samples showe

greater than 100-fold and 10·2% of samples greater than 1,000-fold increase in *coli-aerogenes* organisms, dominated by *Klebsiella* [*Cloaca*] *cloacae* and *K. aerogenes* I. Although some strains of all the *coli-aerogenes* organisms isolated showed growth on yeast-dextrose agar at 3–5°C. in 5 days, the majority of the *K. cloacae* strains grew luxuriantly and can be considered typical facultative psychrophiles of milk. *Betty C. Hobbs*

FOOD POISONING

World Health Organization. Technical Report Ser. No. 184. **European Technical Conference on Food-Borne Infections and Intoxications.** Report. Geneva, 16–21 February 1959. 18 pp. [23 refs.] 1959. Geneva: Palais des Nations. [Sales agent for U.K., H.M. Stationery Office.] [1s. 9d.; $0.30; Sw.fr. 1.–.]

Food-borne diseases are defined as those diseases which can be traced (a) to specific food, substance in the food, or dish which has been contaminated by noxious organisms or substances, or (b) to a particular food-producing or food-dispensing establishment where a contamination has occurred.

The report deals with epidemiological procedures for the investigation of outbreaks, and preventive and control measures which might be adopted by health authorities. There are sections on classification, notification and reporting. Under the heading of epidemiological investigations it is explained that the collection of information from patients, and collection of food samples, are primary requirements, and that international agreement on diagnostic methods to be carried out in well equipped laboratories staffed with competent personnel is advisable.

For control measures, it is stressed that medical and veterinary public health services should co-operate to trace sources of salmonella infection when basic food ingredients such as egg products or meat are concerned; there is not only danger from the consumption of the finished product but also through the risk of spreading the contamination to other products. It is suggested that the country of origin should be informed when imported foods are found to be contaminated. Food premises, and the medical examination of food-handlers are considered, and a section is devoted to methods of health education for all workers in the food-handling industry.

Under the heading of laboratory examination of foods for hygienic purposes, it is recommended that there should be international studies of methods for the bacteriological examination of perishable foods with a view to the provision of standards. Furthermore, there should be international dissemination of information on the bacteriological condition of foods intended for both human and animal consumption.

Annexes include a model form for reporting incidents of food-borne disease, principal features of the different types of food-poisoning, and references.

Betty C. Hobbs

Thatcher, F. S., Comtois, R. D., Ross, Doreen & Erdman, I. E. **Staphylococci in Cheese: Some Public Health Aspects.** *Canadian J. Pub. Health.* 1959, Dec., v. 50, No. 12, 497–503.

During 1957 a survey was made of the distribution of staphylococci in marketed Canadian cheese made from unpasteurized milk, and in pasteurized cheese imported from other countries. Also from factory A, specimens of cheese from 166 vats were examined for enterotoxin, and samples of milk from each contributing herd were examined for staphylococci.

Counts were made on 20 gm. samples of cheese; the coagulase test, phage typing and antibiotic sensitivity were carried out on all staphylococcal cultures. The presence of enterotoxin was investigated by intraperitoneal injection of young adult cats with a heated filtrate (30 minutes in a boiling waterbath) from a 30% suspension of cheese in water.

224 samples of cheese were examined from 80 factories. In 106 (47%) specimens there were less than 100 staphylococci per gm.; in 67 (30%) specimens there were more than 10,000 per gm. Staphylococci were not found in numbers greater than 10,000 per gm. in cheese older than 6 months.

Factory A samples contained staphylococci in numbers greater than 10,000 per gm. in 91 specimens (54%), in 10 (6%) the count exceeded 1,000,000 per gm. The staphylococcal count exceeded 10,000 per ml. in 36 of the 53 herd specimens of milk, and the milk from one herd gave counts which exceeded 1,000,000. The leucocyte count from 9 herds was greater than 500,000 per ml. and the erythrocyte count in the same samples ranged up to 175,000 per ml.

Among the 269 cultures from all sources, 25 were phage type 42D, 209 were of type 42D in association with other phages, and 62 belonged to types known to be associated with human infections. No type 42D strains were antibiotic-resistant.

Enterotoxin was demonstrated by the cat test in 8 of 149 specimens tested from vat samples of cheese. The toxic cheese contained up to 1,500,000 staphylococci per gm. No staphylococci were found among 236 specimens of imported cheese, mostly made from pasteurized milk, or which had been heat-processed after manufacture.

Betty C. Hobbs

Young, W. C. **A Paratyphoid Fever Outbreak.** *Health Bull.* (Issued by the Chief M.O., Dept. of Health, Scotland.) 1960, Jan., v. 18, No. 1, 14–15.

There were 47 cases of infection due to *Salmonella paratyphi B* phage type Taunton in the Borough of Motherwell and Wishaw and adjacent areas during the months May to August, 1959. The common food was artificial cream in various forms of bakery confectionery. A bakery employee who sorted different forms of cream cakes in the dispatch section was found to be excreting *Salm. paratyphi B.*

Evidence for her role as source of infection or victim was inconclusive. Cream and cake samples proved negative bacteriologically, but there was no record of examination of food ingredients; imported frozen whole egg contained *Salm. paratyphi B* phage type Taunton at that time. See CAMERON [this *Bulletin*, 1960, v. 35, 653 and NEWELL, *et al.*, *ibid.*, 1956, v. 31, 315]. *Betty C. Hobbs*

RIDDELL, J., NORVAL, J. & ANDERSON, G. K. **An Outbreak of Salmonellosis in a Cattle Court Dairy Farm.** *Health Bull.* (Issued by the Chief M.O., Dept. of Health, Scotland.) 1959, Oct., v. 17, No. 4, 67–71.

The investigation of this outbreak involved team-work between the Medical Officer of Health, sanitary inspectors, veterinary surgeons of the local authority and control department, bacteriologists, and the general medical practitioner and general practitioner veterinary surgeon. In addition, farm proprietors were fully informed and co-operative.

In January 1958 cases of *Salmonella typhi-murium* infection occurred in the County of Midlothian; there was a common milk supply from a farm with a certified licence distributing through 2 creameries. The 100 cows on the farm were kept in cattle courts with an adjoining milking parlour. 300 dry cows and heifers were housed nearby. 4 weeks before calving the cows were mixed with those in milk, and calving took place in the cattle courts; the growing calves were kept in small pens some distance from the courts. At the time of investigation the trough and drinking bowls were contaminated by dung and the cows ate bedding straw and grain contaminated with rodent excreta from neighbouring stacks infested with mice.

There had been uninvestigated cases of gastro-enteritis among the 4 households supplying the 7 dairy workers on the farm and in 3 other households on the farm drinking the same milk, but unconnected with the dairy work. There had been no bacteriological examinations among the cattle although 4 animals had been acutely ill, scouring either before or after calving, 2 had died and from one *Salm. typhi-murium* had been isolated. Other cows had "chills" and 2 calves were sick. By March, 102 more human cases had occurred; *Salm. typhi-murium* was isolated from dairy and non-dairy workers and their families, and of the total herd of 110 cows, 60 excreted *Salm. typhi-murium* at some time. In March, 4 calves died from the infection. Bulk sampling of the milk was carried out; one sample was positive in January.

Precautions taken were as follows: Infected cows were milked after the others, and the milk destroyed; pasteurization of milk from healthy cows; examination of faeces from all farm employees and their families, and from all cattle; examination of bulk samples of milk and feeding-stuffs, and treatment of the whole herd with one of the nitrofurans and the human carriers with antibiotics.

The actual source of the outbreak was obscure. It is suggested that infection in a carrier animal suddenly flared up with spread to other animals, or that the contaminated grain and bedding may have been responsible. It is emphasized that stress factors, *e.g.*, calving, m cause symptoms of salmonellosis to become manifest a severe form.

It was considered that both animals and humans w probably infected for 2 weeks before the infection v discovered, through general spread into the communi more accurate diagnosis at an early stage in both medi and veterinary fields was desirable. *Betty C. Hobb*

DOLMAN, C. E., TOMSICH, Maria, CAMPBELL, C. C. & LAING, W. B. **Fish Eggs as a Cause of Hum Botulism. Two Outbreaks in British Columl due to Types E and B Botulinus Toxins.** *Infect. Dis.* 1960, Jan.–Feb., v. 106, No. 1, 5– 7 figs. [25 refs.]

In 1957, 3 Indian women at Prince Rupert and 1 Port Edward (British Columbia) died after eating raw s mon eggs containing in the first instance type E toxin *Clostridium botulinum*, and in the second, type B tox *Cl. botulinum*, type E, of feeble toxigenicity was isola from the eggs and the stomach contents of 1 victim the first outbreak. There was evidence that *in v* tryptic activation of the toxin occurred intragastrically all three cases. A more toxigenic type E strain was i lated from eulachon oil collected from the house at same time, but no toxin could be demonstrated in the

In the second outbreak a nonproteolytic strain of *botulinum* type B with spores of low heat resistance w isolated from the salmon eggs; the culture resemb European type B strains, but differed from those of North American type B. Colonial characteristics described. The toxin was enhanced by trypsin *in vi*

From 1919–1958, 46 out of 78 persons affected d in 18 botulism outbreaks in Canada. Fish and mar products were responsible for 10 incidents, caused type E toxin in 6. It is emphasized that trivalent (ty A, B and E) antitoxin should be manufactured and sto in readily accessible depots for emergencies. 6 kno outbreaks of human botulism due to fish eggs from s mon and trout are described, 5 among Indians of No America (Alaska, The Yukon, and British Columbia) 1 in Japan. Public health education is needed to w the Indians of the Northwest Pacific Coast against eat uncooked and non-refrigerated fish eggs. Even the c trolled preparation of caviare in Japan and the U.S.S is not without risk. *Betty C. Hobb*

SUTHERLAND, H. P. **Report of a Case of Botuli Poisoning.** *J. Amer. Med. Ass.* 1960, Mar. v. 172, No. 12, 1266–8.

This paper contains a very full clinical account o case of botulinus poisoning in a woman aged 41 ye The diagnosis was made on the classic symptoms botulism exhibited by her and on the collateral evide that there were the same symptoms in 3 fatal cases i families and in 2 other persons. The source of poison appears to have been slices of "odd-tasting p pared beets" consumed about 28 hours before the f symptoms of difficulty in reading and diplopia w

oticed. None of this jar of beets remained for examiation but a similar jar processed at the same time by e "dangerous open-kettle method" showed marked oilage, and Gram-positive spore-forming rods were seen a smear. The material in this jar was, however, not isonous when injected into unprotected guineapigs.

There is a full description of the stormy course of the isoning complicated by bronchopneumonia in this oman who, however, recovered and was discharged to r home after 23 days. The treatment of the patient nsisted of the administration of 350,000 units of polylent botulinus antitoxin, 8 days in a Drinker respirator, tibiotics (dihydrostreptomycin sulphate, polymyxin B lphate, penicillin, oxytetracycline, oleandomycin phosnate, chloramphenicol, erythromycin, kanamycin sulnate and nystatin were given at various times) and supртive measures. *M. E. Delafield*

NDERSON, L. S. **Toxic Shellfish in British Columbia.** *Amer. J. Pub. Health.* 1960, Jan., v. 50, No. 1, 71–83, 5 figs. [16 refs.]

61 cases of paraesthetic fish poisoning occurred in and hortly after October 1957, among people living along e shores of the Straits of Georgia. 34 of the patients ncerned had eaten oysters, 23 had eaten clams, and 4 ad eaten mussels. Symptoms started with tingling and umbness of the mouth and lips, which was followed by ngling and numbness of the tips of the fingers progressg to numbness and incoordination of the arms. In vere cases tingling and numbness occured also in the es, feet and legs, and in some instances there was incordination of the legs. Recovery took place in 2–3 days. 7 out of 8 cats died within an hour or two of eating ams. 2 dogs ate the clams, they staggered about for me hours, but after vomiting recovered; 8 or 9 racoons were found dead on the beaches of Hornby Island. oxic levels in clams and oysters were high only in the rthern end of the Straits of Georgia, where the sale of l shellfish was banned for 9 weeks, when it was lifted r oysters but not clams, which remained toxic (May, 958). The causal relationship between dinoflagellate hytoplankton and shellfish and the need to predict and control the toxic phenomenon are discussed, together with observations on the diversity of phytoplankton and its place in the cycle of the sea. It is not known, however, which phytoplankton causes the trouble.

The epidemiology and epizoology of the outbreak in relation to net tidal drift, climatic conditions and salmon movement are discussed. The transfer of batches of oysters, clams and mussels between toxic and non-toxic waters is described, and the possibility of using clam styles as plankton indicators is suggested.

The appendix lists the names of 131 species of flagellates found in the Straits of Georgia. *Betty C. Hobbs*

SHAH, K. V., NAVAVATI, A. N. D. & DUTTA, N. L. **Outbreak of Polyneuritis in Bombay with a Syndrome clinically indistinguishable from Tricresyl Phosphate Poisoning and with Demonstration of Tricresyl Phosphate in a Sample of Mustard Oil.** *Indian J. Med. Sci.* 1960, Mar., v. 14, No. 3, 183–9, 5 figs.

In the introduction to this paper there are references to the literature on tricresyl phosphate poisoning, its symptoms and clinical course, and on the more important outbreaks of this poisoning, the most recent of which was in Morocco in 1959 [this *Bulletin,* 1960, v. 35, 241].

There is here an account of 2 episodes in Bombay of illness which, mainly on the evidence of its character, was diagnosed as tricresyl phosphate poisoning. The first episode was in 6 members of a family in whom the illness was ultimately diagnosed although no positive evidence of its chemical origin was obtained after careful investigation. Later the municipal health authorities reported cases of "mustard oil poisoning" in 2 separate localities, in 1 of which there were 9 cases in a single family and in the other 60 cases in 12 to 14 families. Consumption of mustard oil was found to be the common factor in all these cases. Samples of this oil were obtained from shops and tricresyl phosphate was found on chemical examination to be present in 1 of the samples which had been purchased by an affected family. *M. E. Delafield*

Mycoses and Mycology

The order of diseases and fungi in this section is:—**General; Dermatophytes; Blastomyces; Histoplasma; Sporotrichum, Phialophora; Candida, Cryptococcus; Actinomyces, Nocardia; Aspergillus; Others.**

Papers on Blastomycosis (South American type), Coccidioidomycosis, Mycetoma and Rhinosporidiosis are abstracted in the TROPICAL DISEASES BULLETIN.

RINCE, H. N. **Effect of *p*H on the Antifungal Activity of Undecylenic Acid and its Calcium Salt.** *J. Bacteriology.* 1959, Dec., v. 78, No. 6, 788–91, 1 fig.

Optimal fungicidal activity of certain fatty acids is ssociated with a low *p*H, but the authors of this article found that the effect of *p*H on the fungicidal activity of such long-chain fatty acids as undecylenic acid had not hitherto been studied. In this paper they record the results of such a study.

Broth adjusted to various *p*H values was added to tubes containing various amounts of undecylenic acid or its calcium salt, and then inoculated with 0·1 ml. of a

suspension of aerial growth from slope cultures of various dermatophytes. These tubes were then incubated at 25°C. and read after 10 days.

Glucose-tryptose agar was also poured into Petri dishes and inoculated likewise with dermatophyte suspension. Measurements of colony diameter were recorded for each *p*H value after 10 days.

The effect of *p*H on respiration was determined by manometric methods.

It was shown that at *p*H values lying between *p*H 4·5 and 6·0 the antifungal action of a given quantity of the calcium salt of undecylenic acid compared favourably with that of an equivalent quantity of the free acid, but that at values above *p*H 6 this degree of antifungal activity was not maintained. For example, at *p*H 7 100 μgm. of the free acid was sufficient to inhibit the growth of *Trichophyton mentagrophytes* whereas at this *p*H value it required a level equivalent to 140 μgm. of available acid for the calcium salt to bring about this result.

C. J. La Touche

Jeremiasse, H. P. Griseofulvine-behandeling bij 50 lijders aan schimmelaandoeningen. Voorlopige mededeling. [**Griseofulvin Treatment of 50 Cases of Mycosis; Provisional Results**] *Nederl. Tijdschr. v. Geneesk.* 1960, Apr. 16, v. 104, No. 16, 762–5, 6 figs. [15 refs.]

The English summary appended to the paper is as follows:—

"A provisional report is presented on 50 cases of mycosis, which were treated with griseofulvin for a period of 24 weeks. A marked clinical improvement was effected, and microscopic examinations were often negative. The period of observation was too short to yield any definite information on the chances of recurrence or re-infection."

Cremer, G. Ervaringen over de behandeling van mycosen met griseofulvine. [**Treatment of Mycosis by Griseofulvin**] *Nederl. Tijdschr. v. Geneesk.* 1960, Apr. 16, v. 104, No. 16, 766–73, 6 figs. [14 refs.]

The English summary appended to the paper is as follows:—

"Fifty-eight cases of dermatomycosis were treated with 1 g. griseofulvin daily, with no local therapy. Of these 58, 2 patients with favus capitis were cured in 4 and 2 months respectively. A subacute tinea capitis of 5 months' standing caused by *Trichophyton tonsurans* was cured in 7 weeks. Tinea of the fingernails was cured or considerably improved after 4 months; tinea of the toenails responded more slowly and less completely. The skin in concomitant chronic tinea of the hands and feet was usually free from fungus in 1-2 months. In this group of 18 patients, 9 relapses were seen 1-9 weeks after 4 months' therapy had been discontinued, mostly on the soles of the feet or in the interdigital clefts, but in 2 cases in the fingernails. Vesiculous tinea pedis showed a favourable response to griseofulvin, but tended to relapse in obstinate cases. Tinea of skin covered with lanugo was cured completely. Pityriasis versicolor chronic thrush of the oral mucosa were not influenced griseofulvin therapy."

Earle, J. H. O., Highman, J. H. & Lockey, Eunice. **Case of Disseminated Histoplasmosis.** *Brit. M J.* 1960, Feb. 27, 607–11, 4 figs. [34 refs.]

These authors describe the 4th case of disseminated histoplasmosis occurring in Britain.

The patient, who was aged 62 years, was English, had spent 30 years in India. On admission he gave history of having lost 4½ stones in weight, of anore and "great lassitude." An ulcer on the tongue been removed as also was some granulation tis around the anus.

On examination, his liver and spleen were just palpable; a healed scar was present on the dorsum of tongue; he had lost weight; he was very drowsy; X- examinations did not reveal any abnormalities in lungs. Laboratory findings did not include any abn malities in the blood picture other than a sustained h sedimentation rate. Liver function tests revealed abn malities which were attributed to excessive alcoh intake. The patient deteriorated rapidly after the f week, and laboratory findings then indicated a re lesion and hepatic failure.

Despite sustained therapy and despite a partial temporary response to it during which the patient's cli cal condition improved, a terminal progressive deteri tion set in and the patient died at the end of 2 mon after admission.

At autopsy it was found that the ulcer on the dors of the tongue had returned. Besides this, the pathol ical features were: in the liver, a multilobular type cirrhosis; in the adrenals, an almost complete alterat due to enlargement and to various destructive proces in the kidneys large lesions were present in the medull region.

Histological investigation revealed numbers of his plasma organisms in the yeast phase situated in macrophages of the granulation tissue of the ton lesion and of the anal lesion, and likewise in the tiss of the adrenals and the medulla of the kidneys. histoplasma organisms were found in the liver or in spleen. Culture was not performed. *C. J. La Touch*

Viswanathan, R., Chakravarty, S. C., Randha H. S. & deMonte, A. J. H. **Pilot Histoplasmo Survey in Delhi Area.** *Brit. Med. J.* 1960, F 6, 399–400.

As a result of the report of a case of histoplasm from Poona by Kalra *et al* [this *Bulletin*, 1957, v. 1199] the authors of the present article carried ou survey in order to ascertain the possible incidence benign histoplasmosis in the Delhi area.

Persons above the age of 5 years were tested in dermally with histoplasmin. Reactors were subjected physical, radiological and laboratory tests which inclu serological tests, blood culture, bone marrow biopsy culture of bronchial aspirates.

" 12·3% positive reactors were found in the riverine ea, 2·9% in the rural area, and 4·9% in the urban ea."

All cultural and serological examinations of these posi- e reactors were negative. *C. J. La Touche*

e also p. 775, ENGELKE, HEMPHILL, BUSHELL & MCKINNEY, **A Survey of Tuberculin and Histoplasmin Reactors among School Children of Washtenaw County, Mich.**

ROCKNOW, J. J., PAGE, M. I. & LOOSLI, C. G. **Early Pathogenesis of Experimental Histoplamosis.** *Arch. Pathology.* 1960, Apr., v. 69, No. 4, 413–26, 20 figs. (16 coloured) on 4 pls. [20 refs.]

SCHMIDT, E. L. **Cultural Conditions influencing Nitrate Formation by** *Aspergillus flavus. J. Bacteriology.* 1960, Apr., v. 79, No. 4, 553–7, 2 figs.

FOLEY, J. M., BERMAN, R. J. & SMITH, C. E. **X-Ray Irradiation of** *Coccidioides immitis* **Arthrospores: Survival Curves and Avirulent Mutants Isolated.** *J. Bacteriology.* 1960, Apr., v. 79, No. 4, 480–87, 7 figs. [30 refs.]

[An abstract of this paper appeared in the *Tropical Diseases Bulletin*, 1960, v. 57, 847.]

Communicable Diseases

The order in this section is:—**Tuberculosis; Venereal Diseases; General Infective Diseases; Other Communicable Diseases.**

For the bacteriology of these diseases see the section on Bacteriology below. For diseases conventionally regarded as tropical, readers are referred to the TROPICAL DISEASES BULLETIN.

TUBERCULOSIS

OBAR ACOSTA, M. I. Investigación de tuberculosis en colectividades. El metodo en Colombia. [**The Investigation of Tuberculosis in Communities. The Colombia Method**] *Rev. Facul. de Med.* Bogotá. 1959, Mar.–Sept., v. 27, Nos. 3/9, 129–44. [15 refs.]

The theme of this paper is that it is no longer adequate limit epidemiological investigations to a diagnosed ase of tuberculosis and to work outwards to find new ases among the contacts. The modern method is centipetal working from the periphery towards the foci of ifection. There are probably more undiscovered than nown cases and new cases must be sought among the eneral community, especially among those sections of it ost likely to harbour the disease. This can best be one by mass miniature radiography which in this paper called abreugraphy ("*abreugrafía*") after Manoel de bréu, the Brazilian who devised it. Its advantages are: leads to a fuller knowledge of the course of the disase; it discovers abnormal conditions other than tuberulosis; it finds patients with tuberculosis at an earlier tage than do ordinary clinical methods; it can operate n every part of a country ; and its cost is relatively low. By the Abréu method 60 to 100 films an hour can be aken. Figures are quoted from many countries where nuch miniature radiography is done. For success o-operation of the general public is essential. In Latin America the disease progresses rapidly. The findings of he radiological units must be followed up and existing nti-tuberculosis measures cannot be neglected or educed.

Figures are given of the work of the 23 miniature radiographic units now operating in Colombia. Few work to full capacity: the figures vary from 60·5 to 96·2%. In 1955, 581,862 persons were X-rayed out of a population of about 13,227,480 and it is estimated that 131 units in all are needed to cover the whole population.

In 1950, 3,692 cases came to light from all sources and in 50·0% the lesions were advanced and in 16·7% minimal. In 1956 the total number was 7,218 but among them 44·0% were advanced and 21·7% minimal. Even the latest figures of new cases found are low for a poor country and point to the need for a more determined effort to look more diligently for new cases especially in the urban and suburban areas. *Allen Daley*

JEURISSEN, A. La situation actuelle de la tuberculose infantile en Belgique. [**Childhood Tuberculosis in Belgium**] *Bruxelles-Méd.* 1960, Apr. 10, v. 40, No. 15, 519–27.

Between 1930 and 1956 tuberculosis death rates per 100,000 children in Belgium fell from 98·4, 29·6 and 19·2 in the age-groups 0–1, 1–5, and 5–15 years respectively to 10·9, 4·1 and 1·4. The actual numbers of children of each group who died in 1956 were 16, 23 and 17 respectively; the principal cause of death was meningeal tuberculosis.

The number of notifications of meningitis at all ages fell by 52% between 1950 and 1957 and that of bone

and joint tuberculosis by 35%. The decline in meningitis was greatest at 10–30 years of age. The number of cases of bone and joint tuberculosis fell in all age-groups from 3–40 years but since 1953 there has been a marked increase after the age of 40 and a slight increase at 1–3 years.

It is more difficult to assess the change in morbidity from pulmonary tuberculosis but this can be done in the group aged 16–21 years since they are subject to pre-employment and repeated annual X-ray examination until the age of 21. The discovery rate of pulmonary tuberculosis in this group has fallen by 85% in 7 years. Further evidence of the decline in morbidity is shown by the falling tuberculin reactor rate in the schools. Tuberculin conversion is no longer the inevitable fate of children as they grow up.

Bovine tuberculosis will have been eradicated by 1962, and human sources of infection are being controlled. Nevertheless in 1958–59 2 school epidemics of tuberculosis involving 30 children were reported. The infector in each was a teacher who had refused X-ray examination.

The tubercle bacillus is as virulent as ever, and the only reason why advanced lesions are rarely seen in children is that frequent routine examination detects the disease at an early stage. Every initial reactor is a potential case of active tuberculosis, and disease develops in 1 in 10 reactors. Extra-familial infection is more often responsible for the spread of disease to children than infection within the household. The most dangerous infectors are persons who are already known to have tuberculosis but are not under adequate treatment or supervision. The tuberculous person to-day is no longer confined to bed but is to be found in general circulation endangering his contacts especially if they are children. All known patients should be given adequate and prolonged chemotherapy. *H. G. Calwell*

Pedrini. I. Epidemiologia della tubercolosi nella Regione Trentino-Alto Adige nel decennio 1947–1956. [**The Epidemiology of Tuberculosis in the Region of Trentino and Alto Adige during the 10 Years 1947–1956**] *Lotta c. la Tubercolosi.* 1959, Nov., v. 29, No. 11, 1515–49, 27 figs. French & German summaries. Discussion 1550–52.

This survey was carried out in the 2 provinces of Bolzano (360,000 inhabitants) and Trento (404,000 inhabitants), which are in mountainous country. The population of Trento Province is partly Italian (one-third), the rest are mostly German-speaking and some 30,000 of these live in isolated mountain communities.

Economic, housing and other environmental circumstances which have a bearing on the incidence and course of tuberculosis, and the health and social services which are locally available to deal with the disease, have been covered by this survey. There are 3 dispensaries and 320 hospital beds for the disease in Bolzano Province and 6 dispensary centres and 2,600 hospital beds in Trento Province.

The death-rate from tuberculosis in Bolzano Province was 0·7 per 1,000 in 1947, had been more than halved (0·3 per 1,000) 2 years later and remained at 0·2 per 1,000 in each of the last 3 years covered by the survey. Trento Province the figures are higher and the impr ment less marked—0·9 per 1,000 in 1947 and 0·4 per 1 in 1956—with no obvious explanation.

In both provinces the course of improvement in morbidity rate from the disease has been less steady c the 10 years under review and the authors comment this from the point of view of the continued spread infection. While benefiting the individual patient arresting his illness and prolonging his life through action of antibiotic and other new drugs, we may at same time be preserving, and even adding to, the num of infective sources. By the end of 1956, 56·8% of cases which had been ascertained in Bolzano Provi during the first 5 years covered by the survey, and 67· of those in Trento Province had become clinic arrested. [It is not stated if any, or how many, of th remained "open."]

The authors report, and comment on, the distribut and forms of tuberculosis, and its association with cosis. They discuss social class of the groups wh have or have not accepted the grants made availa through national assistance.

In conclusion, they warn against placing sole relia on the new curative drugs, which still leave and m indeed, preserve the chronic case as a source of int tion. We must continue to fight tuberculosis by empl ing the traditional measures of prophylaxis, ascert ment, cure, after-care and family assistance and associ them with such more recent measures as the immuni tion of those who are particularly exposed to the risk contracting tuberculous infection. *J. Cauch*

Ekblom, B. & Frisk, M. **The Mortality in P monary Tuberculosis in Mental Hospitals Finland.** *Acta Tuberculosea Scandinavica.* 19 v. 38, No. 2, 153–67, 2 figs. [16 refs.]

This is a study of the tuberculosis death rates in mental hospitals in Finland between 1920 and 1955 relation to the rates in the entire population.

The total number of patients was 4,767 of whom 1, died; 378 (32·5%) died of tuberculosis. Excluding p ents under 20 and over 74 who were few in numb observation years in the study numbered 23,676.

The periods of comparison are 1920-30, 1931-40, 19 45 (a period of extreme starvation owing to the w 1946-50 and 1951-55.

The death rate from pulmonary tuberculosis for m in the normal population fell continuously through the period except during the war. The rate in the 195 was about one-third of that in the 1930's. The decl was greater at 20-39 years than in older groups.

The mortality rate in male mental patients increa very much during the war and was slow to decline. was greatest in the group below 40 for all periods exc the 1950's. During the period 1930-50 the rate w higher in younger patients than in older but the oppos prevailed in 1951-55 after the advent of chemothera A separate analysis of schizophrenic patients was ma

In the general female population there was a stea decline in the tuberculosis death rate to one-sixth of

920 figure. The decline was greater in younger than in older persons. The rate in female patients declined steadily also to about one-third. During all periods the rate was highest in early adolescence. The conditions of starvation which so seriously affected the mortality rates in men had no significant effect on the rates in women. In all periods the tuberculosis death-rate was higher in the mental patients than in the general population, with one exception. *H. G. Calwell*

FERRIS, M. & MONK, Mary A. **The Validity of Socio-Economic Differentials in Tuberculosis Mortality.** *Amer. Rev. Respiratory Dis.* 1960, Apr., v. 81, No. 4, 513–17. [10 refs.]

The inverse relationship between tuberculosis mortality and social class is well known. In this paper the authors have tested the hypothesis that this relation is due in part to the disease causing a lowering of the social status of the persons attacked. The data used were the deaths of the residents of Buffalo occurring during the years 1949–51. The address of the deceased persons was traced to varying periods back to 1925. The city was divided into four grades based on rents and these groups were taken as the index of the economic position of the residents. Of the 380 male deaths and 113 female deaths 61 males and 11 females could not be traced; 42 of the 61 untraceable males were in the lowest social grade. A comparison of the social grade at death and that at the earliest traced showed no significant difference and this was true for the 324 persons traced back to 1925–35, *i.e.* 15–25 years before death. This study produced no evidence that the excess deaths in the low income groups was the result of a downward shift in social class during life caused by the disease.

W. J. Martin

See also p. 766, SELTSER & SARTWELL, **The Application of Cohort Analysis to the Study of Ionizing Radiation and Longevity in Physicians.**

See also p. 754, SCHUDEL [**A Study of the Relation between Silicosis and Tuberculosis in a Foundry**].

ENGELKE, O. K., HEMPHILL, Fay M., BUSHELL, Elizabeth & MCKINNEY, E. Belle. **A Survey of Tuberculin and Histoplasmin Reactors among School Children of Washtenaw County, Mich.** *Amer. J. Pub. Health.* 1960, Mar., v. 50, No. 3, Pt. 1, 368–76, 1 fig.

The objects of this survey were to obtain a picture of the distribution of sensitivity to tuberculin and histoplasmin, to discover cases of tuberculosis in reactor children and their families and to find out if histoplasmosis was distributed unevenly within the county surveyed.

The survey took place in two months of 1958 in south east Michigan (U.S.A.); 19 schools with 13,037 pupils were selected. The Mantoux test was used with 5 TU of PPD-S, and the dose of histoplasmin injected (also intracutaneously) was "0·1 ml. of a 0·001 ml. of United States reference standard antigen." The criterion of a positive reaction to either test was induration of at least 6 mmm. at 2–3 days.

The total number of children tested was 9,098, comprising 7,370 white, 1,650 Negro and 78 other children. The overall acceptance rate was about 70% (37–92%); it was highest among elementary school children and lowest among senior high school children.

15·8% were tuberculin-negative but histoplasmin-positive, 0·2% reacted to both antigens. The reactor rate to histoplasmin was very much greater in 1 well-defined area than elsewhere being 9 times higher than in a contiguous area. There was evidence that histoplasmin sensitivity is independent of tuberculin sensitivity.

Approximately 3 times the rate of positive tuberculin reactors was found in Negroes compared with whites. The rate of positive reactions to histoplasmin was less in Negroes than in whites.

Reactors to tuberculin in all schools were X-rayed but reactors to histoplasmin were X-rayed only in the village of high incidence. There was evidence of tuberculosis in 29·4% and of histoplasmosis in 24·6%.

Further investigation of the distribution of histoplasmosis is recommended. *H. G. Calwell*

TACQUET, A., GAUDIER, B. & PECQUEREAUX, J. P. Étude comparative du B.C.G. test pratiqué chez l'homme avec des bacilles sensibles ou des bacilles résistants à l'isoniazide. [**The BCG Test in Man with Strains Sensitive or Resistant to Isoniazid**] *Ann. Inst. Pasteur de Lille.* 1958–1959, v. 10, 51–60, 1 graph.

The authors have compared BCG skin tests in man using ordinary vaccine and vaccine prepared from strains of BCG rendered resistant to 10 or 100 ugm. of isoniazid. The method of preparation of the resistant strains is described.

108 tuberculous patients under treatment with isoniazid were tested with heat-killed sensitive and resistant BCG by scarification and intracutaneous injection. Induration was measured on the 2nd, 7th, 15th and 25th days.

With scarification 7 tests were negative and 101 positive. 3 of the patients who failed to react were under treatment with corticosteroid.

With intracutaneous injection both tests were negative in only 1 patient; this patient was not suffering from tuberculosis. 15 of these patients were receiving corticosteroid treatment; the reaction in half of these was retarded until the 15th day.

There was no difference in the degree of reaction to scarification whether the strain of BCG was resistant or sensitive to isoniazid. On the contrary reactions to intracutaneous injection were more intense and appeared earlier with the resistant than with the sensitive strain.

40 non-tuberculous patients suffering from conditions such as bronchial carcinoma, lung abscess, bronchiectasis or asthma were tested with living resistant or sensitive BCG. Each group consisted of 10 patients receiving isoniazid and 10 not receiving isoniazid. The results with both vaccines were identical. *H. G. Calwell*

American Rev. Respiratory Dis. 1960, Apr., v. 81, No. 4, 482–4. **Recommendations of the Arden House Conference on Tuberculosis.**

The major goal proposed is the sterilization by widespread chemotherapy of the reservoir of tubercle bacilli that exists throughout the country in persons currently suffering from active tuberculous disease, whether known or unknown to the public health authorities, and in selected persons who previously have had active disease and were inadequately treated.

The emphasis in this programme is primarily on the control of infection and the protection of the community; the benefit to the individual is secondary.

The next recommendation is that special attention should be paid to those segments of the population with the greatest tuberculosis problem.

All tuberculosis programmes should be reviewed periodically to take account of changing conditions and new knowledge, and the U.S. Public Health Service should assist and supervise within the states in order to promote uniformity. Laboratory services adequate for all necessary bacteriological investigations should be available to all physicians engaged in tuberculosis work.

BCG vaccination should be practised according to the recommendations of the Ad Hoc Advisory Committee on BCG [this *Bulletin*, 1958, v. 33, 224]. This committee advised BCG for medical and nursing personnel, contacts, and patients and staff of such places as mental hospitals.

Research should be intensified into social, psychological and cultural factors affecting such matters as the susceptibility of the individual to tuberculosis, acceptance of case detection and treatment and the nature and results of treatment programmes. Research should also be intensified to find a simple and accurate tuberculin test suitable for use by non-medical personnel. The current isoniazid prophylaxis field study of the U.S. Public Health Service should continue until it is complete.

H. G. Calwell

Matthews, J. H. **IX. Pyrazinamide and Isoniazid used in the Treatment of Pulmonary Tuberculosis.** *Amer. Rev. Respiratory Dis.* 1960, Mar., v. 81, No. 3, 348–51.

The use of pyrazinamide in the treatment of pulmonary tuberculosis has been extensively studied by the Veterans Administration-Armed Forces investigators. By 1956 it appeared that perhaps the combination of pyrazinamide with isoniazid was a more effective therapeutic regime than any of the double-drug regimes in which isoniazid, PAS or streptomycin were used. This study sets out to determine whether the combination of isoniazid with pyrazinamide would demonstrate sufficient therapeutic superiority to justify its use despite the hazard of hepatoxicity.

Reports cover the first 4 months of treatment. Two groups of essentially comparable patients were treated by 2 regimes. 237 patients were treated with isoniazid 300 mgm. daily, and PAS 12 gm. daily, and 219 patients were treated by isoniazid 300 mgm. daily, and pyrazinamide 3 gm. daily. Neither by comparison of X-ray changes, or cavity closure, or reversal of infectious was any statistical superiority of the pyrazinamide reg demonstrated.

An attempt was made to evaluate the relative effect ness of PAS and pyrazinamide in preventing the er gence of bacilli which were resistant to isoniazid. early results favoured isoniazid-PAS, and the later res are slightly better with isoniazid-pyrazinamide. At end of 9–12 months, however, out of 84 patients on isoniazid-PAS regime only 6 were still expectora bacilli, and of the isoniazid-pyrazinamide group 2 ou 48 patients were excreting tubercle bacilli.

Toxicity sufficient to require discontinuing H occurred in 19 patients (7%) of the 267 who origin started to take these drugs. Of these, 13 had to have PAS stopped because of gastrointestinal intolerance, 6 patients because of hypersensitivity.

Pyrazinamide therapy was discontinued in 35 pati (13%) of the 261 who were given the isoniazid-py inamide combination, plus 2 others who had renal d culties. Of the 35 toxicity reactions, 21 patients de loped hepatocellular dysfunction manifested by abnor liver function tests, and another 6 were clinically ja diced. 6 others had gastrointestinal symptoms wh may have been prodromal symptoms of hepatic dise

Treatment was stopped because of toxicity attribu to isoniazid in 1 patient in the isoniazid-PAS group, in 4 patients who received isoniazid-pyrazinamide.

It is concluded that the pyrazinamide-isoniazid gr had no statistically significant advantage over the iso azid-PAS group, and the very definite appearance hepatoxicity made it inadvisable to use the pyrazinam group as a routine method of treatment. *F. H. Youn*

Berte, S. J. & Bowen, Clotilde D. **An Evaluation Chemotherapy in Pulmonary Tuberculo High Doses of Isoniazid and PAS versus Da Streptomycin with High Doses of Isoniazid a PAS.** *Amer. Rev. Respiratory Dis.* 1960, M v. 81, No. 3, 407–11.

Several investigators have recently expressed the o ion that the most effective chemotherapy in pulmon tuberculosis consists of daily streptomycin, and h doses of isoniazid with adequate concentrations of logically active isoniazid in the blood [this *Bulletin*, 1 v. 33, 218; 1959, v. 34, 326]. This study was desig to observe the effectiveness of treatment employing h doses of isoniazid along with PAS, in comparison w high doses of isoniazid along with both daily strep mycin and PAS. Group A received isoniazid 1 mgm. per kgm. per day, and PAS 12 gm. per day. Gr B received streptomycin 1 gm. daily for 90 days, iso azid 10-20 mgm. per kgm. per day, and PAS 12 per day. All patients in both treatment groups recei also 100 mgm. of pyridoxine daily.

After sundry deductions, 113 patients were avail for Group A, and 92 patients for Group B. The c centrations of free isoniazid in the blood were consid adequate in nearly all patients in the study biologic assayed. Only about 7% of all patients had value isoniazid of less than 0·3γ per ml. but the clin

esponse was just as effective in these cases as in the 3% with higher concentrations of isoniazid in the blood.

An analysis of treatment in all cases revealed the following: when high doses of isoniazid along with PAS re used in the treatment of pulmonary tuberculosis, nd when adequate concentrations of free isoniazid are btained, the use of daily streptomycin for 90 days in ddition to the other drugs does not produce any signifiantly superior therapeutic results. 7 patients were ound to excrete tubercle bacilli noted to be resisant to 1 or more drugs, but all the 7 patients demontrated very satisfactory responses to treatment and early eversal of infectiousness. Toxicity to streptomycin 10% in 120 patients) was primarily responsible for a ·6% higher incidence of drug reactions in the triple rug treatment group; however the percentage of patints in whom 1 or more drugs had to be discontinued as only 2·8% higher in the triple drug group than in he 2-drug regime group. 99-100% of all 205 patients n both groups had cultures persistently negative for ubercle bacilli after 5-6 months of observation.

F. H. Young

PEER, E. T. **The Treatment of Tuberculosis with Alternating Drugs.** *Amer. Rev. Respiratory Dis.* 1960, Mar., v. 81, No. 3, 415–18. [Refs. in footnotes.]

In the spring of 1954, the author of this paper was nhappy about treatment failures in tuberculosis, and it ccurred to him that it might be possible to obtain better esults if 2 drugs were used together in not more than month, and then followed by the use of 2 different lrugs the following month. An important influence on he author's thinking was provided by previous experince with syphilis. Recently several reports of rotating lrug regimes have been published [this *Bulletin,* 1953, v. 28, 1032; 1956, v. 31, 1085] but the regime used in the present observation was somewhat different. Streptonycin 1 gm. was given 3 times weekly with 3 gm. of PAS 4 times daily for the first month of treatment. This was alternated on a monthly basis, with 100 mgm. of soniazid 4 times daily, and 1 gm. of pyrazinamide 3 imes daily. Later the dose of streptomycin for the first month was increased to 1 gm. daily. If intolerance leveloped, cycloserine was substituted for the offending drug, and the alternating schedule thus modified was continued.

The first patient was treated in April 1954, and 3 others were added shortly; this had to be abandoned as pyrazinamide became unobtainable.

The paper presents 83 previously untreated patients with pulmonary tuberculosis, all of whom had been treated for at least 6 months on an alternative regime, except the first 4 original patients who had received somewhat shorter chemotherapy. The period of observation varied from a maximum of 5 years to a minimum of 10 months; there were rather more males than females. Usually isoniazid and PAS were continued at home after discharge for a varying period of up to 2 years on the drugs. Of the total, 65 had tubercle bacilli in sputum or gastric washings at some time during observation. In 41 patients the sputum contained tubercle bacilli only before treatment or during the first month of treatment. In 9 patients the sputum was infectious after 1 month, but not thereafter; in 5 it remained infectious after 2 months; in 4 after 3 months, and in 5 after 4 months of treatment. Thereafter the sputum remained non-infectious in all but 1 patient in whom reversal of infectiousness required 7 months. 17 non-pulmonary primary treatment patients were also treated in this way, with satisfactory results.

50 more patients were treated on an alternating regime, but are excluded from the 100 already reported because other anti-tuberculous drugs had been used before the alternating treatment was begun, or for other reasons.

As regards toxicity, streptomycin produced the most difficulty, requiring a substitution in 22 cases. The PAS required substitution in 15 cases, cycloserine in 9, pyrazinamide in 7, isoniazid in 3, and oxytetracyline in 1 case. Pyrazinamide was not stopped in a single case because of liver damage. Cycloserine, which was used very much less frequently, offended more often.

Although X-ray clearing has been good it is believed that attention should be primarily directed to sputum conversion and absence of relapse rather than X-ray clearing.

Of the 100 previously untreated patients, 68 are back at work, 14 others have left hospital, and 2 are dead from non-tuberculous causes.

The author does not stress the use of any particular drugs, but he suggests that effective drugs should be used in full therapeutic doses, and these effective drugs should be used in such a way that 2 drugs are used by monthly alternation with 2 different drugs, and that this regime should be continued until the maximum clearing has taken place as shown by stable X-ray findings.

[100 tuberculous patients are mentioned in the summary, so presumably the 17 non-pulmonary primary treatment patients are added to the 83 previously untreated patients with pulmonary tuberculosis.]

F. H. Young

GREGG, J. A. & MAYOCK, R. L. **Thrombocytopenia induced by Administration of Sodium Para-Aminosalicylate.** *J. Amer. Med. Ass.* 1960, Apr. 23, v. 172, No. 17, 1909–12, 3 figs. [15 refs.]

SAEED, A. H. **Our Experience of Anti-Biotics and Chemo-Therapeutics.** *Pakistan J. of Health.* 1959, Oct., v. 9, No. 3, 174–88.

This paper deals with the results obtained by various combinations of antimicrobial drugs in the treatment of pulmonary tuberculosis, carried out at the Sardar Bahadur Khan Sanatorium at Quetta.

The paper commences with a short account of some points in the pathology of tuberculosis, and then has a review of various methods of treatment in other centres. The author then reports on 401 cases classified as fit, maximum benefit, and dead. Regimes are divided into 5 groups, each group being classified by the extent of the disease, toxicity, etc. The various groups have wide divergencies in the number of patients dealt with. The group results are then compared. Group III which commenced

with intravenous PAS gave the best results; in this group the intravenous PAS was followed by the usual course of antibiotic chemotherapeutic treatment. Surprisingly enough, a group in which tebafen was substituted for isoniazid was found to give satisfactory results. Another surprising observation was that a long 7-week course of vitamin A—50,500 I.U. (Arovit)—one tablet once a week going up to 7 tablets in the last week, brought about complete disappearance of symptoms and return of hearing in cases of streptomycin toxicity. [The paper does not state whether the bacteriological results were obtained by smear or culture.]

An interesting account is given of the results obtained in this centre in Pakistan, but some readers will find the paper a little difficult to follow in its conclusions.

F. H. Young

United States Pub. Health Service: **Tuberculosis Therapy Trials. Preliminary Observations from a Controlled Trial of Prednisolone in the Treatment of Pulmonary Tuberculosis.** *Amer. Rev. Respiratory Dis.* 1960, Apr., v. 81, No. 4, 598–600, 2 figs.

"In preliminary observations after twelve weeks of treatment in a controlled trial of prednisolone as an adjuvant to antimicrobial therapy of pulmonary tuberculosis, a five-week course of the steroid was superior roentgenographically and equal bacteriologically to a placebo. On the other hand, a 9-week course of steroid, while also superior roentgenographically to the placebo, resulted in less rapid reversal of infectiousness. Results also confirm earlier findings on the superiority of daily streptomycin-pyrazinamide over isoniazid-PAS as initial therapy."

Jesiotr, M. & Lavon, E. [**Treatment of Pleurisy with Effusion with Steroids**] *Harefuah.* Jerusalem. 1960, Apr. 1, v. 58, No. 7 [in Hebrew 226–7. (12 refs.) English summary 227–8].

The English summary appended to the paper is as follows:—

"Different methods, such as bed rest, pleural puncture, diaphragmatic exercises, have failed to shorten the duration of the disease, or prevent the complications of severe pleural adhesions and empyema. Anti-microbial drugs, while curtailing the length of disease, were of no use in the prevention of adhesions.

"In our cases, treatment with steroids together with antimicrobial drugs, caused the complete disappearance of the pleural exudate within a period of 10–14 days. No adhesions appeared. The movements of the diaphragm were unhindered. There were almost no signs of deterioration of lung function.

"The steroids were applied both locally (inoculation of hydrocortisone into the pleural cavity) and orally (meticorten), for 2-3 weeks only. We obtained good results in all early cases which we treated during the past 2 years. No complications connected with this treatment could be observed.

"In our opinion steroids plus antimicrobial drugs are the treatment of choice in pleurisy with effusion."

Gernez-Rieux, C., Gervois, M. & Nistri, Résultats éloignés des premières vaccinations ar tuberculeuses (B.C.G.) d'Albert Calmette effectue à Roubaix, de 1925 à 1934. Étude comparati jusq'en 1959 de la mortalité tuberculeuse chez sujets vaccinés à la naissance et chez les sujets nc vaccinés. [**A Long-Term Follow-Up of Calmette Original Series of BCG Vaccinations**] *Ann. In Pasteur de Lille.* 1958–1959, v. 10, 89–96, 2 grap

Roubaix is an industrial town in the north of Fran where Calmette began vaccination of the newborn w oral BCG. The vaccine was given by midwives in th routine care of the infants (3 doses of 10 mgm. at int vals of 48 hours in the first 10 days of life). Eve effort was made to vaccinate the infants of tuberculc families, and the vaccinated group therefore contains majority of infants exposed to infection within the fam from birth.

From 1925 to 1951 18,586 infants were vaccinated c of a total of 49,883 born in that period. The autho have confined their study to those born in 1925-34 these were aged 24—34 years at the time of the follow- and would have passed through the age of greatest s ceptibility to tuberculosis before the era of speci chemotherapy.

The number followed up was 18,405 of whom 12,5 had not been vaccinated and 5,810 had been vaccinat Among the vaccinated were 1,490 who had been revac nated at the age of 1 year and 153 who had been vaccinated a second time at 3 years.

Children who died of tuberculosis in the 1st year life are excluded from the analysis as they were consider to have been infected before the vaccine could ha exercised a protective effect.

The tuberculosis death rates per 1,000 in the remaini vaccinated and unvaccinated infants were respectively 0 and 1·2 from 1–4 years, 0·4 and 0·9 from 5–9, 0·8 a 0·9 from 10–14, 0·8 and 1·4 from 15–19 and 0·4 a 1·1 after 20. These differences obtained for all forms tuberculosis.

This result was obtained in spite of the small dose vaccine given and the unfavourable environment of children. The prolonged protection afforded by vacci tion is amply demonstrated. *H. G. Calwel*

Gernez-Rieux, C., Gervois, M., Nistri, R. Lebeurre, R. Protection conférée contre la tub culose au cours des dix premières années suiva la vaccination B.C.G. par scarifications cutané [**The Protective Effect of BCG Vaccination Scarification—A Ten Years' Follow-up**] *A Inst. Pasteur de Lille.* 1958–1959, v. 10, 97–120 graphs. [18 refs.]

Since 1947 the authors have been engaged in assess the long-term value of BCG vaccination in Lille. Earl stages of their study have been noticed in the *Bull* [1952, v. 27, 1019; 1954, v. 29, 265; 1955, v. 30, 8 1959, v. 34, 328].

Schoolchildren aged 6–14 years and numbering 22,9 participated; none was in contact with a known sou of tuberculous infection and all had normal chest sk grams. 15,567 who did not react to the Mantoux t

10 TU) were vaccinated by scarification with BCG (75 mgm./ml.). There were 2 control groups: 3,173 children who did not react to the Mantoux test (in duration less than 5 mm.) and were left unvaccinated and 4,165 children who were reactors. The last group was sub-divided according to the degree of tuberculin sensitivity.

Annual re-examination included X-ray examination and tuberculin testing. 88·2% were examined in 1956 and 76·8% in 1958–59. The mean ages in January 1959 of the vaccinated and unvaccinated non-reactors were 19 years and 20 years respectively, and of the original reactors 20 years.

There was little difference in the incidence of non-tuberculous morbid conditions in the 3 groups. Death rates from such conditions were 0·4, 0·6 and 0·5 respectively.

Active tuberculosis was discovered in 257 persons—81 vaccinated, 107 unvaccinated non-reactors and 69 unvaccinated reactors. There was a reduction of 83·7% in the morbidity rate in the vaccinated group compared with the group of unvaccinated non-reactors.

Protection was most effective against the early forms of the disease such as primary complexes, peritonitis, meningitis and peripheral adenitis. There was however considerable protection against later forms such as destructive pulmonary tuberculosis; the reduction in this form was 66·6%. There was no waning in protection throughout the period of observation. No meningitis occurred in the vaccinated group; there were 3 cases in the second group.

It was found that tuberculosis occurring in the vaccinated was often less serious and more easily cured than in the others.

The incidence of tuberculosis in the group of original reactors was 3½ times greater than in the vaccinated group; pulmonary tuberculosis was 6 times more frequent. It was also more extensive and less tractable. Persons with an initially low degree of tuberculin sensitivity were less likely to develop destructive pulmonary tuberculosis than those with initially high sensitivity.

The authors estimate that if all non-reactors in the series had been vaccinated with BCG there would have been a total reduction in morbidity of 61%. Considerably greater reduction could be obtained by vaccinating at an earlier age when the natural reactor rate is lower.

H. G. Calwell

VENEREAL DISEASES

Nicol, C. **Homosexuality and Venereal Disease.** *Practitioner.* 1960, Mar., v. 184, No. 1101, 345–9.

This author reports investigations on this subject at 2 venereal disease clinics (St. Bartholomew's and St. Thomas's Hospitals, London) and quotes figures from St. Mary's Hospital. In 1954 at one clinic 10 out of 838 patients were homosexuals compared with 40 out of 813 in 1959; in 1959 at a larger clinic 262 out of 4,258 were homosexuals (6·1%); of these 18 had syphilis, 148 gonorrhoea, 43 non-gonococcal infection, and 53 no venereal disease. Of 225 patients, 112 were between 20 and 29 years old and 66 between 30 and 39; 212 were British, 10 other white, and 3 coloured; 7 were married and 218 single; the large majority did light or sedentary indoor work. Of 183 patients with venereal disease, nearly twice as many had penile as anal lesions *i.e.*, were "active" partners.

Thus it appears that more homosexuals are contracting venereal disease than formerly and that diagnosis of anal infection in the passive homosexual is difficult unless suspicion is aroused; the health authorities should inform the public that venereal disease may not uncommonly follow homosexual practices. *T. E. Osmond*

Garzón, R. & Ferraris, A. Superinfección luética: un caso documentado sobre una lúes primaria. [**Syphilitic Superinfection. A Case Recorded in the Primary Stage**] *Rev. Facul. Ciencias Med.* Cordoba. 1959, Oct.–Dec., v. 17, No. 4, 309–14, 4 figs. [15 refs.] English summary.

Heymann, G. & Steiger, Irmgard. Das "Allgemeine Standardprinzip" in der quantitativen Serodiagnostik der Lues. II. Mitteilung. Einführung einer Internationalen Reagin-Einheit. ["**The General Standard Principle" in the Quantitative Serological Diagnosis of Syphilis: II. Introduction of an International Reagin Unit**] *Ztschr. f. Immunitätsf. u. Exper. Therap.* 1960, Jan., v. 119, No. 1, 95–109, 7 figs. [18 refs.]

The importance of a standard serum of reference to be used in all comparative work on WR serum titres is emphasized.

The German standard serum L.1, presumably a solution of powdered lyophilized product, has a solid content of 79·4 mgm./ml. and the standard international serum RP has one of 31·7 mgm./ml. The ratio of activities of these products is 1 of L.1 = 3·8 of RP. The reagin unit of the German product has been found to be 2·384 mgm. and that of the international standard serum 3·617 mgm. [For previous studies see this *Bulletin*, 1957, v. 32, 850.] *J. W. McLeod*

Bossak, H. N., Duncan, W. P., Harris, A. & Falcone, Virginia H. **Assay of Tests for Syphilis on Unheated Serum.** *Pub. Health Rep.* Wash. 1960, Mar., v. 75, No. 3, 196–8.

These authors compared the Rapid Plasma Reagin test on unheated serum (RPR-US) (which was the same as the RPR test but with serum instead of plasma) and the

unheated serum reagin test (USR) with the VDRL test on specimens from a variety of sources. Of 592 specimens from presumably normal persons, 2 were reactive with each test but represented 4 different specimens, all of which were TPI positive; in 6 different varieties of syphilis the 2 unheated serum tests agreed closely with one another but were considerably more reactive in treated primary, treated secondary and treated latent syphilis than VDRL; in conditions other than syphilis VDRL gave only half as many positive reactions as the other 2; in biological false positive sera negative with TPI all 3 tests gave 47 to 48% reactions and in those which had not been tested by TPI the percentages were 50, 50, and 44 respectively.

It is not very clear what conclusions can be drawn from the above except that the RPR-US and USR tests appear to be sensitive but by no means highly specific.

T. E. Osmond

LYNCH, F. W., KIMBALL, Anne C. & KERNAN, P. D. **Serologic Tests for Syphilis following Smallpox Vaccination and including Reiter Protein Complement Fixation Technic.** *J. Investigative Dermat.* 1960, Mar., v. 34, No. 3, 219–22.

It is well known that recent vaccination may cause classical serum tests for syphilis (STS) to become positive in the absence of the disease. These authors submitted sera from normal persons who had been vaccinated within the previous few weeks to 3 STS, using lipoidal antigen (Hinton, Kahn and Kolmer Wassermann), to 3 using cardiolipin antigen (Kline, VDRL and Kolmer WR), and to the Reiter Protein Complement-Fixation Test (RPCF). The sera were obtained from 212 persons, 97 having primary and 115 accelerated vaccinia; 44 of the former (45·4%) and 13 of the latter (11·3%) gave positive reactions with one or more of the routine tests and only one gave a partial reaction with RPCF (this was probably a technical error and a repeat test was negative). In primary cases the Hinton, Kahn and Kline gave most reactions (40 to 21%); in accelerated cases, the order was much the same but the percentage of positive reactions was only 7·9 to 1·7%. In general sera taken 19 to 22 days after vaccination were more often reactive than those taken later. Data from 5 cases are given and the detailed results are set out in 3 tables. Thus the RPCF appears to be highly specific.

T. E. Osmond

KJELLANDER, J., SIEVERS, O. & VOGELSANG, T. M. **The Reiter Protein Complement Fixation Test for Syphilis (RPCF) compared with the** *Treponema pallidum* **Immobilization Test (TPI) in a Selected Material.** *Acta Path. et Microb. Scandinavica.* 1959, v. 47, No. 4, 373–9. [19 refs.]

These two tests were compared in two different laboratories, namely Gothenburg and Bergen; in the former, there were 161 sera from patients with syphilis and 123 from patients presumed free from syphilis; in the latter there were 165 and 80 sera respectively. All the TPI tests were carried out at Gothenburg, and the RPCF tests at Bergen. Detailed results are set out in 9 tables. In t syphilitic sera both tests were positive in 76·1% and bo negative in 8·2%; TPI only was positive in 9·2% a RPCF only positive in 6·5%; in the non-syphilitic se the respective positive and negative percentages were 2 and 60·6; TPI only was negative in 21·0% and RPC only in 6·9%. In early syphilis RPCF was positive i cases which were negative with TPI, but TPI was mo often positive in treated late cases of syphilis. The RPC gave more inconclusive results than the TPI, but in oth respects results were comparable. [However in table it appears that TPI gave more negative results in no syphilitic sera than did RPCF.] *T. E. Osmond*

BROWN, W. J., PRICE, Eleanor V. & SIMPSON, W. **The Reiter Protein Antigen Test compared wi the TPI and other Treponemal and Nontr ponemal Antigen Technics in the Diagnosis Syphilis.** *J. Investigative Dermat.* 1960, Mar., 34, No. 3, 223–6, 3 figs. Discussion 226–7.

The particular test in question is designated KR (Kolmer Reiter Protein) which was compared with oth tests; results of this test in 2 series show in the fi series reactivity rates of 78, 45 and 91% in untreat early, treated early, and adequately treated, late ca of syphilis; in the second series the figures were 42, 2 and 31% for untreated, inadequately treated, and the combined, respectively.

When KRP was compared with 4 other tests the p centages of reactions (estimated from the illustration were (a) in untreated early syphilis KRP 78, VDRL 8 TPCF 79, FTA 77 and TPI 64; (b) in treated ea syphilis the corresponding figures were 45, 13, 45, 38 a 41; (c) in adequately treated late syphilis the figures we 91, 84, 85, 92 and 97.

In another series the respective figures were (a) in u treated syphilis, 42, 42, 88, 87, and 93; in inadequate treated syphilis the figures were 22, 17, 82, 74, and 8 total syphilitics, including adequately treated, the figu were 32, 28, 83, 80, and 90. [The figures in these paragraphs are estimated from histograms in the text.]

All "reactions" include "weak reactions"; it is n stated what the FTA test is and it appears that KR and RPCS (Reiter Protein Complement-Fixation Te are not exactly the same.

It is stated that Reiter Protein tests and TPI ga similar results in syphilis and show specificity rates 96·0 and 96·2 but Reiter Protein tests should be inte preted with caution, particularly in the case of elde patients. *T. E. Osmond*

VAISMAN, A. & HAMELIN, A. Nouvelle méthode sérodiagnostic de la syphillis *in vivo*, ou phénomè de Pfeiffer appliqué à *Treponema pallidum*. **New Method of** *in vivo* **Serodiagnosis in Syphili or application of Pfeiffer's Phenomenon to** *Tr ponema pallidum*] *Ann. Inst. Pasteur.* 1959, Sep v. 97, No. 3, 420–24.

The test here described is essentially the same as t TPI test but carried out *in vivo* rather than *in vitro*.

uspension of *Treponema pallidum* in saline (100-million per ml.) is added to the heated serum to be tested in the proportion of 4 ml. to 1 ml. and kept for half an hour at 37°C.

The mixture is then injected into the peritoneal cavity of a guineapig. After 4 and again after 7 hours fluid is withdrawn and examined under the microscope; if the reaction is positive all spirochaetes will have disappeared, if negative they will remain. Of 106 sera examined, 39 which had given negative classical and TPI reactions were all negative; 46 known syphilitic sera or cerebrospinal fluids were all positive; 7 gave inconclusive results; 5 biologically false positive sera were all negative; sero-positive primary was negative; 4 syphilitic sera which gave unsatisfactory results with TPI were all positive; 4 sero-negative sera which gave unsatisfactory TPI reactions were all negative. The advantages of this test are: no survival medium is necessary, spirochaetes need not be motile or even alive, sterility is not important and results are available where TPI fails; disadvantages are the large numbers of spirochaetes needed, the necessity to use 1 guineapig for each test and the difficulty of applying the method to large numbers of tests. This test should be most useful when TPI results are unsatisfactory for various reasons. [See also TANI *et al.*, this *Bulletin*,, 1956, v. 31, 628.] *T. E. Osmond*

BAKKER, P. G., ESSEVELD, H. & LEIKER, D. L. Nieuwere ervaringen bij de gonorroe-behandeling. [**Recent Experiences in the Treatment of Gonorrhoea**] *Nederl. Tijdschr. v. Geneesk.* 1960, Jan. 9, v. 104, No. 2, 65–6. [11 refs.] English summary (9 lines).

In July 1958, 20 cases of relapsing gonorrhoea were observed in the Seamen's Hospital in Rotterdam. Some of the patients were foreign seamen in whom treatment with penicillin had failed, and the disease in the remainder did not clear up after a single injection of 600,000 units of procaine penicillin. Tests of sensitivity to penicillin were carried out on gonococci isolated from 12 patients with relapse of gonorrhoea and from 15 suffering from recent infections; 8 strains grew in the presence of 0·1 unit per cc. and 3 resisted 0·3 unit per cc. 9 of the resistant strains were isolated from patients suffering from relapses. *D. J. Bauer*

JORGENSEN, L. **Lymphogranuloma Venereum. A Study of the Pathology and the Pathogenetic Problems based on Observation of Eight Cases examined Post Mortem.** *Acta Path. et Microb. Scandinavica.* 1959, v. 47, No. 2, 113–39, 14 figs. [70 refs.]

This author studied 8 cases of the disease very carefully and reports his results and gives his views, comparing those with the views of many others. In a table are set out case histories, laboratory findings, causes of death and autopsy findings. Of the 8 patients, 2 were males and 6 females, the average age at death was 60 and the average duration of the illness 26½ years. 7 had rectal stricture and 1 polyserositis; inguinal adenitis only occurred in 3 cases. As regards pathology, lymph nodes were filled with large mononuclear cells transformed into abcesses; plasma cells were also numerous and fibrosis was observed. Rectal strictures were funnel-shaped (narrowest above), and varied greatly in length and circumference. The inflammatory process involved the intestinal wall and adjacent tissue; microscopically the epithelium was lost and the inflammatory tissue was similar to granulation tissue. The liver appears to be susceptible to the virus and pyelonephritis or pyelitis is common.

The development of the disease is caused by the virus penetrating the reticulo-endothelial cells causing great proliferation; large mononuclear giant and perhaps plasma cells result; necrosis follows and abcesses form. Three questions require answering: (1) What is the role of lymph stasis? (2) How does the virus reach the rectum? (3) How does the inflammatory process proceed in the wall of the intestine? Lymph stasis is not primarily essential but dilatation is prominent; the virus usually reaches the rectum *via* the surface but also through the lymphatics; stricture may be caused by swelling of the mucosa and even muscle spasms; in the late stages by fibrous contraction. This is a notable contribution to the literature and deserves careful study; there are 14 figures, mostly photomicrographs.

T. E. Osmond

WARNER, H. A., MARTIN, J. R. & CAMERON, D. G. **Reiter's Syndrome occurring in the Female. Report of a Case showing the Complete Triad and Other Features.** *Canadian Med. Ass. J.* 1960, Apr. 23, v. 82, No. 17, 886–7, 1 fig.

CATTERALL, R. D. & NICOL, C. S. **Is Trichomonal Infestation a Venereal Disease?** *Brit. Med. J.* 1960, Apr. 16, 1177–9. [18 refs.]

A study of the literature shows that the large majority of observers consider that *Trichonmonas vaginalis* (TV) infection is nearly always venereally acquired; however there is a possibility that it may be acquired in other ways, *e.g.*, from fomites, swimming baths, and perhaps from lavatory seats. The authors investigated 56 couples who admitted recent sexual intercourse and in all of whom the organism was found; the average age of the men was 33 and of the women 24; 30 were married couples, 24 were friends and 2 were casual acquaintances (admitting only 1 sexual intercourse). 6 couples were found to have gonorrhoea. For diagnosis, wet smears were examined routinely and cultures were carried out in many cases; examination of an early morning urethral scrape and of centrifuged urine should "increase the number of positive cases." The authors favour the theory of venereal transmission and think all cases should go to a Venereal Diseases clinic where contact tracing could be carried out; sexual intercourse should be forbidden until both partners are clear. *T. E. Osmond*

GENERAL INFECTIVE DISEASES

The order in this section is:—**General; Hospital and other Cross Infections; Coccal Infections; Bacterial Infections; Virus Infections.**

GENERAL

RIGAL, CAUSSE, BLANCHARD, DUCROS & TOURTIER. Les complications neurologiques des vaccinations. (A propos de 13 observations personnelles.) [**Nervous Complications of Vaccinations (13 Personal Observations).**] *J. Méd. de Bordeaux.* 1960, Apr., v. 137, No. 4, 397–9.

That post-vaccination complications involving the central nervous system are of comparatively rare occurrence is exemplified by the authors' experience in encountering only 13 such complications among the hundreds of thousands of persons immunized after recruitment for service with the French army during the past 5 years. These 13 complications followed the administration of one or other of the following vaccines: anti-rabies, TABDT, anti-typhus and anti-yellow fever. Distribution of the cases according to the type of vaccine used and the part of the central nervous system affected is shown in tabular form below.

	Vaccine used			
Part affected	Anti-rabies	TABDT	Anti-typhus	Anti-yellow-fever
Cerebral hemispheres	—	1	1	1
Cerebellum	—	1	—	—
Spinal cord	2	1	—	—
Nerve roots	—	2	2	—
Meninges	—	—	—	2

All parts of the central nervous system were, therefore, involved—a variety in localization of the nervous complication paralleled by the wide range of symptoms observed.

Commenting on their cases, the authors find themselves unable to regard the occurrence of these complications as mere coincidence because of the fact that the time-interval between the administration of any one particular vaccine and the onset of nervous symptoms was significantly regular. Predisposition to such complications might be expected in persons who had suffered from some previous nervous disorder or, because such complications are commonly regarded as being allergic in character, in persons with a history of previous allergy. Of the 13 cases, however, only 2 persons had had earlier affections of the nervous system and none a history of previous allergy. On the basis of this latter observation, therefore, it would be impossible to recognize before vaccination those persons liable to tolerate immunization badly and thus become subject to later nervous complications. Inasmuch as in TABDT and anti-typhus vaccination, for example, nervous complications have been observed to occur more especially after revaccination, care should be taken to avoid needless vaccination in persons already immunized. *G. Stuart*

GARDNER, P. S., STANFIELD, J. P., WRIGHT, A. E., COURT, S. D. M. & GREEN, C. A. **Viruses, Bacteria, and Respiratory Disease in Children.** *Brit. Med. J.* 1960, Apr. 9, 1077–81. [19 refs.]

146 children with acute respiratory illnesses we examined by clinical, bacteriological and virologi methods. All children were admitted to hospitals Newcastle-upon-Tyne from January 1 to June 30, 19 They were divided into 5 clinical groups consisting (1) 28 patients with acute respiratory infections (cory pharyngitis, tonsilitis, otitis media); (2) 6 with croup, 37 with acute bronchitis, (4) 27 with acute bronchioli and (5) 48 with bronchopneumonia or segmented pne monia.

Coagulase-positive *Staphylococcus aureus, Haem philus influenzae, Streptococcus pneumoniae* and *Str pyogenes* were isolated from a number of patients but relationship was demonstrated between any single or nism and any one of the clinical groups.

Infections by influenza A virus (3 patients), influen B virus (17 patients), influenza C virus (3 patients), cro associated virus (5 patients), adenovirus (6 patients) a Sendai virus (2 patients) were detected by virus isolati or serological methods. None of these viruses were p ticularly associated with any of the clinical groups b no evidence of any virus infection could be detected any of the children with acute bronchiolitis.

H. G. Pereira

HOSPITAL AND OTHER CROSS INFECTIONS

FLECK, A. C., Jr. & BOUTON, M. **Staphylococcal Ou breaks in Infants detected after Hospital D charge.** *Pub. Health Rep.* Wash. 1960, Ja v. 75, No. 1, 11–14, 1 chart. [14 refs.]

Records were made by public-health nurses at routi visiting of newborn infants after discharge from 3 mat nity hospitals in New York State of the frequency skin sepsis. In a 3-month period sepsis was recorded 18 (2·9%) of 610 babies. The survey also revealed t occurrence of an epidemic of infection due to *Staphy coccus aureus* type 80/81; subsequent examination of 233 infants born in the hospital in the relevant peri discovered 20 cases (8·6%) of suppuration and one dea The epidemic ended spontaneously and the source w not discovered. *R. E. O. Williams*

NATIONAL RESEARCH COUNCIL: **Associate Committ on Control of Hospital Infections** [MURR E. G. D., Chairman]. **Staphylococcal Infectio in Canadian Hospitals.** *Canadian Med. Ass.* 1960, Feb. 20, v. 82, No. 8, 403–6, 1 fig.

This brief paper summarizes reports from 45 hospit in Canada on the incidence of staphylococcal infecti

eveloping in patients in hospital. In 153,835 patient-dmissions in 6 months, there were 1,354 (0·88%) active nfections and 397 (0·26%) doubtful infections. For urgical services the incidence of active infection was ·43% and for medical services 0·84%. 1,264 (2·29%) f 55,068 surgical patients had infection present on dmission.

[The rates for staphylococcal infection of surgical patients are much lower than many that have been reported from elsewhere. No details are given of the method of collecting the information, or of assessing its reliability; there is no indication of the number of patients having surgical operations, nor of the proportion of the infection in surgical wards that was wound infection.]

R. E. O. Williams

FOSTER, W. D. **Environmental Staphylococcal Contamination. A Study by a New Method.** *Lancet.* 1960, Mar. 26, 670–73, 4 figs. [16 refs.]

The distribution and numbers of *Staphylococcus aureus* on the floor of hospital wards were determined by the use of impression cultures on agar slabs strengthened with gauze. It was shown that a patient infected even with a small lesion could rapidly contaminate a wide area of floor, and an infected patient could continue to disperse staphylococci for a long period. The current method of floor-cleaning with 1/80 Sudol was found not to be very effective in killing staphyloccoci; 1/40 was much better.

R. E. O. Williams

MANFIELD, Pauline A., SHOOTER, R. A. & LIDWELL, O. M. **Nasal Staphylococci and Sepsis in Newborn Babies.** *Brit. Med. J.* 1960, Apr. 9, 1098–9.

Of 110 babies who had triple dye applied to the umbilical stump, and who had nasal swabs taken daily during their stay in hospital, 35% left hospital on the 12th day without having become nasal carriers of *Staphylococcus aureus*. When an ultraviolet air disinfector was installed in the nursery the proportion (on 97 babies) was 36%, despite the fact that the numbers of *Staph. aureus* in the air were reduced by one-half to two-thirds. Of 105 babies washed daily with the proprietary hexachlorophane preparation, Phisohex, 46% were not nasal carriers on discharge.

24 (7·7%) of the 312 babies suffered staphylococcal sepsis, the numbers in the 3 treatment groups being 7, 11 and 6. 10·5% of the babies who were nasal carriers on discharge developed sepsis, compared with 3·3% of those who were not. *R. E. O. Williams*

COCCAL INFECTIONS

The order in this section is:—*Staphylococcus, Streptococcus, Neisseria, Others.*

PATERSON, W. I. & BURNS, G. C. T. **Staphylococcal Infection in Christchurch in 1958.** *New Zealand Med. J.* 1959, Dec., v. 58, No. 328, 787–91.

Swabs were taken from consecutive septic lesions presenting to general practitioners in Christchurch, New Zealand, and examined for staphylococci, which were isolated from 179. 97 strains (54%) were resistant to penicillin, 13 being resistant also to streptomycin and chlortetracycline as well. 72 strains (40%) were type 80/81; 28 were type 3C/55/71.

Only 6% of the patients had been in hospital within the previous 6 months, compared with 5% of the total population of the area; the proportion infected with type 80/81 was however 63% for those who had been in hospital or had some other hospital contact, compared with 36% for those without hospital contact. [Nevertheless only 19 of 72 patients with 80/81 had recognized hospital contacts.] *R. E. O. Williams*

HAY, D. R. **Pulmonary Manifestations of Staphylococcal Pyaemia.** *Thorax.* 1960, Mar., v. 15, No. 1, 82–8, 10 figs.

Of 73 patients suffering from staphylococcal septicaemia, 33 (44%) developed pulmonary complications. Metastic subpleural abscesses consisting of haemorrhagic consolidation associated with small air-filled cysts were the usual findings. Radiologically these appear as round low density shadows from 0·5 to 1·5 cm. in size usually in the middle zone of the lungs. In the early stage there may be only one such shadow but usually a film taken a few days later will show new ones. The commonest sign was increased respiratory rate, there were frequently scattered rales but cough was not common. The patients were treated with prolonged courses of penicillin or with combinations of erythromycin and novobiocin: the mortality rate was 45% but in only 1 case was the pulmonary complication regarded as the primary cause of death.

A. B. Christie

PARISH, H. J. & CANNON, D. A. **Staphylococcal Infection: Antitoxic Immunity.** *Brit. Med. J.* 1960, Mar. 12, 743–7. [38 refs.]

This is a general review of the clinical evidence for the importance of toxin in staphylococcal infection, toxoid in prophylaxis, and antitoxin in treatment. Very little of the evidence is critically quantitative.

R. E. O. Williams

BACTERIAL INFECTIONS

The order in this section is:—*General, Corynebacterium, Haemophilus, Enteric bacteria, Brucella, Pasteurella, Bacillus, Anaerobes, Spirochaetes, Others.*

SCHUCHARDT, L. F., MUNOZ, J. & VERWEY, W. F. **Studies on a Combined Diphtheria-Pertussis-Tetanus-Poliomyelitis Vaccine.** *Amer. J. Pub. Health.* 1960, Mar., v. 50, No. 3, Pt. 1, 321–8. [20 refs.]

There are obvious advantages in being able to combine in one series of injections antigens protecting against diphtheria, tetanus, whooping cough and poliomyelitis. Results of inoculating such a combination together with sufficient potassium alum to adsorb the antigens from solution into animals are presented. It was found that the addition of poliovaccine did not interfere with the antibody response produced by diphtheria and tetanus toxoids in guineapigs or by pertussis in mice. The response of monkeys to poliovaccine on the other hand was definitely enhanced by combination with the other antigens. Tests on the stability of the combined vaccine showed that it remained potent for 8–12 months at 2–5°C. The results of trials of this quadruple antigen developed by Merck Sharp and Dohme, West Point, Pa., (Tetravax) in man are to be presented later. [See also this *Bulletin*, 1958, v. 33, 1112.] *A. J. Beale*

PRZEGLĄD EPIDEMIOL. Warsaw. 1959, v. 13. No. 3, 223–48, 1 fig. Zaraza duru brzusznego w domach akademickich w Krakowie w roku 1957. [**Typhoid Epidemic at Student Hostels in Cracow in 1957**] English summary.

In 1957 an outbreak of typhoid with a total of 176 cases occurred in Krakow, Poland, in 4 students' halls of residence which used the same refectory. The incidence in the individual halls ranged from 9·7 to 16·6%, and 9 of the 25 kitchen staff contracted the disease. The outbreak was traced to a cook who was found to be a typhoid carrier. 2 cases were fatal. An attempt to control the epidemic by giving chloramphenicol prophylactically was unsuccessful. *D. J. Bauer*

ELIAKIM, M. **Electrocardiographic Signs of Pericarditis in Typhoid Fever.** *Amer. J. Med. Sci.* 1960, Apr., v. 239, No. 4, 492–7. [12 refs.]

"Electrocardiographic signs of pericarditis were observed in 3 patients with typhoid fever. In 2 of the cases the changes were preceded by electrocardiographic evidence of myocardial involvement, usually found in typhoid fever. In one case the changes were characteristic of 'pure' pericardial involvement. The changes of pericarditis were observed during a relapse in one case, and during the second or third week of the disease in the other 2 cases. In all cases they appeared after defervescence, and in 2 cases lasted 4 to 5 days; in one case they lasted more than 2 weeks. No clinical or roentgenographic evidence of pericarditis was found and no specific treatment was required."

KLUGMAN, H. B. **Reactions to T.A.B. Injectio** *South African Med. J.* 1960, Jan. 23, v. 34, No. 64.

[The usual reactions to TAB vaccine are local, which there may be various degrees of disability d to local pain and swelling, and constitutional disturbanc related to the subcutaneous injection of any foreign an gen. Neither of these types of reaction is specificall related to the particular type of antigen injected an it is extremely difficult to associate any one clinical mar festation specifically with TAB vaccine, but because the frequency of both local and general reactions aft subcutaneous injection of the vaccine and its widespre use there is often a tendency to attribute almost eve illness that occurs after the inoculation to the TA vaccine. It is appreciated, however, that a severe gener reaction may precipitate the clinical onset of a dorma virus infection: clinical herpes has been seen on sever occasions after TAB inoculations. Patients in the inc bation stage of a common cold may sometimes show th complete clinical picture much earlier than might b expected.] The author quotes conjunctivitis in 7 cas (4 were unilateral) after the first dose of TAB; the pos bility of the vaccine activating, or precipitating the ons of, an adenovirus infection might be considered here.

The author's reasons for presenting this paper a that there are very few references in the literature reactions following TAB inoculations. [While this ma be true with regard to papers dealing specifically wit this subject, there are many scattered references in th vast literature concerned with prophylactic measur against enteric fever and very much more informatic which, although it may not have been published, commonly known to all workers experienced in th field.] *H. J. Bensted*

RUYS, A. C. De salmonella-epidemie van deze zome **[Salmonella Epidemic of the Summer of 195** *Nederl. Tijdschr. v. Geneesk.* 1959, Nov. 21, v. 10 No. 47, 2399–401.

During the last few decades a reversal has taken pla in the relative proportions of typhoid and paratypho among the number of enteric infections in the Nethe lands. The incidence of typhoid has gradually falle from more than 2,000 cases annually in 1905-19 to 8 cases in 1956 and 1957 and 77 cases in 1958, where the incidence of paratyphoid has shown a reverse tren and has risen steadily from around 100–200 cas annually between 1931 and 1943 to 3,204 cases in 195 the rise since 1951 being particularly steep. The pos war increase is ascribed to the importation of infecte powdered egg and animal products. The species mo frequently encountered have been *Salmonella typhimu rium, Salm. bareilly* and *Salm. dublin*, and pigs are present the most important source of human infection Outbreaks of salmonella infection in the summer of 19

ere mostly confined to families; they usually followed e ingestion of very large numbers of the organisms, rmally in meat, and contact infections were infrequent. here was no concomitant increase in the number of ses of typhoid or paratyphoid. *D. J. Bauer*

ENZE, B. Zur Ruhrepidemiologie in der Grossstadt mit besonderer Berücksichtigung der Ausscheiderfrage. **[The Epidemiology of Dysentery in Big Towns with special Reference to the Problem of Carriers]** *Zent. f. Bakt.* I. Abt. Orig. 1960, v. 177, No. 3, 353–64, 2 figs.

The problems presented by bacillary dysentery, which the most prevalent of all intestinal infections, were nsidered in relation to the refugee situation in West erlin in a previous paper [this *Bulletin*, 1959, v. 34, 237]. In the present paper the author reports on his rvey of the epidemiology of bacillary dysentery in neral in West Berlin in the period July 1954 to July 957. In this period a total of 1,368 persons were found be infected with Sonne dysentery. A table gives the gures. The peak year was 1955 when 216 patients with e disease and 314 excreters of the organism were found. There is description and discussion of the results of he investigation of this material in respect of age distriution of the cases, group infection and incidence of the fection in hospital staffs and in persons engaged in the od industry. Particular study was made of the period uring which Sonne organisms continued to be excreted, nd the results are set out in a table. For example mong over 500 patients, 72·4% were still excreting the rganisms 5 days after the first isolation, 12·2% for over 0 days and 3·9% were not clear after 30 days. In a few stances the carrier state has persisted for as long as years.

During the period under review Flexner dysentery orgaisms were isolated from only 84 and Schmitz organisms Shigella dysenteriae 2] from 3 persons.

M. E. Delafield

ICKARBY, G. A., COOPER, G. N., MCAVAN, T. & COCKERILL, J. E. **An Outbreak of Bacillary Dysentery.** *Med. J. Australia.* 1960, Jan. 16, v. 1, No. 3, 81–5.

The outbreak of Sonne dysentery described in this paper ccurred in a small township in Victoria with a popula on of about 2,000 and in which sanitation was primitive. he origin of the outbreak was not discovered but 3 ases of infant gastro-enteritis, which were not examined acteriologically, were probably the first clinical mani estations although it is fairly obvious that the infection as already present in the community and that these ases were contracted from a symptomless excreter, or t any rate an undisclosed person who was excreting the rganism. There were no further clinical cases until 6 eeks later when the main epidemic started with 4 cases n infants and gradually built up so that a total of 321 ases were known to have occurred. The epidemiological attern appears to have been fairly typical of an outbreak f Sonne dysentery beginning in young children where, as the infection spreads, parents and other adults become involved so that at the height of the epidemic there are more clinical cases of dysentery among the adults than among the children. Then as the epidemic dies down it is seen that the infection persists longer in the lower age-groups than in adults.

This particular outbreak is of interest as it is a good example of the difficulty of investigating and controlling a highly infectious epidemic in an isolated community where laboratory and other investigational facilities are limited and the population itself apathetic.

H. J. Bensted

SZMUNESS, W. Ergebnisse der eigenen Beobachtungen über Ätiologie und Epidemiologie der chronischen Ruhr. **[Observations on the Aetiology and Epidemiology of Chronic Dysentery]** *Ztschr. f.d.g. Hyg. u. ihre Grenzgebiete.* Berlin. 1960, Apr., v. 6, No. 4, 237–41.

Chronic dysentery patients who may be a source of acute infections are here defined as those who have had the acute disease, established by bacteriological investigation, who after 3 months suffer relapses or some deterioration in their condition and are found to have dysentery organisms in the faeces.

There is here an account of investigations carried out during several years on patients with dysentery in several large hospitals. Chronic dysentery was found to occur on average in 8–9% of all cases and its incidence was particularly high in children up to 4 years of age. An analysis was made of the social circumstances and previous medical history of 195 children with chronic dysentery in comparison with 102 children who had had acute dysentery which did not become chronic. It was found that the majority of the children with chronic dysentery were in families living in bad housing and sanitary conditions. Undernutrition was much more frequent in the experimental than in the control group of children and the chronic dysentery children also had a history of having suffered much more from various infectious and non-infectious diseases.

It was found that organisms isolated from the chronic dysentery children were resistant to sulphonamides in 92% and to antibiotics (syntomycin and lewomycin) in 29% whereas the corresponding percentages in the control group of children were 53% and 13%.

There is a considerable discussion of the problem of chronic dysentery including the subjects of the carrier state and family incidence. *M. E. Delafield*

ROSSI, J. P. & BRANDT, I. K. **Transient Granulocytopenia of the Newborn associated with Sepsis due to *Shigella alkalescens* and Maternal Leukocyte Agglutinins. A Case Report.** *J. Pediatrics.* St. Louis. 1960, May, v. 56, No. 5, 639–47, 1 fig. [40 refs.]

LAVECK, G. D., DE LA CRUZ, F. & KIRSCHVINK, J. **Sulfadimethoxine in the Treatment and Prevention of Epidemic Shigellosis.** *Antibiotic Med.* New York. 1960, Feb., v. 7, No. 2, 119–24. [11 refs.]

This long-acting sulphonamide was used in the treatment of an outbreak of Sonne dysentery among 72 mentally retarded children in one section of a school. By the 9th day of the outbreak 61 of them were affected. 67 of the 72 children with, or exposed to, the infection were treated with sulphadimethoxine 1 gm. initially and then 0·5 gm. daily for 8 days, this dosage being used for those under 80 lb. in weight and doubled for those over that weight. 34 children (50%) were clinically well within 3 days after onset of the illness, and all patients had normal temperatures and absence of diarrhoea within 8 days. *Sh. sonnei* was isolated from school cultures of 7 children (about 10%) 1 month after the therapy, but a second course of the drug resulted in negative cultures. It is concluded that sulphadimethoxine can be an effective drug in Sonne dysentery, when the organism is sensitive to it. [In an outbreak in another section of the school the *Sh. sonnei* recovered showed resistance to the drug.]

H. Stanley Banks

Slone, D. & Levin, S. E. **Hypertonic Dehydration and Summer Diarrhoea.** *South African Med. J.* 1960, Mar. 12, v. 34, No. 11, 209–13, 2 figs. [25 refs.]

Severe attacks of diarrhoea are frequent in South African children showing protein malnutrition [this *Bulletin*, 1957, v. 32, 415]; in the majority dehydration is associated with hypotonicity of the extracellular fluid, but a minority (13% in the present series) show hypertonicity, which is defined as a serum sodium level exceeding 145 mEq. per litre. The authors calculate that hypertonic dehydration probably occurs in 5–6% of diarrhoeal infants in South Africa, but quote incidences ranging from 16–25% in the U.S.A.

The aetiological factors leading to this form of dehydration are stated to be:—(1) diarrhoeal stools of low electrolyte content, (2) deficient water intake, (3) increased insensible water loss *via* lungs and skin, due to high fever and often superadded metabolic acidosis, and (4) ingestion of solutions or milk feeds of high electrolyte content.

The 11 infants described in this report ranged from 2–10 months in age, of whom 7 showed a good state of nutrition, 2 were fairly nourished and 2 ill-nourished. The skin turgor was normal in 7, in 3 the skin and subcutaneous tissues felt "doughy" and in 1 only the skin was markedly inelastic. In 9 neurological abnormalities were present, comprising irritability, stupor, tetany, convulsions or coma. Respiratory disease was evident in 6 patients. On admission, the biochemical findings were as follows:—

	Per litre	Normal range
serum sodium	145–162 mEq.	132·3 ± 6
plasma chloride	106–148 mEq.	98 ± 7
serum potassium less than	4·7 mEq.	5·5 ± 0·8
CO_2 combining power	4·5–11·6 mEq.	18·7 ± 4
blood-urea	74–290 mgm. per 100 ml.	less than 35 per 100 ml.

Treatment was based on the intravenous infusion of 0·2% sodium chloride in 5% invert sugar in quantities of 80–100 ml. per lb. bodyweight every 24 hours. Wh the urinary output was good, potassium chloride w added to the infusion at a concentration of 27 mEq. litre. The alimentary infection was treated with chlo mycetin (chloramphenicol) palmitate 30–50 mgm. per body-weight per day, and for chest infections 250,0 units of penicillin were administered every 6 hours. C feeds were resumed only when the serum electrolyte lev had reverted to normal.

Only 1 child out of this series of 11 died.

The authors quote investigations which demonstr that the kidney of the infant, under water depleti shows a markedly reduced glomerular filtration rate, w increased tubular reabsorption of electrolytes, wher in the adult deprived of water, the glomerular filtrat rate is maintained at nearly normal levels. The rai blood urea in this series is a clear manifestation o reduced glomerular filteration rate.

Hypertonic dehydration is to be suspected in any inf showing severe diarrhoea with marked hyperpnoea a minimal clinical signs of dehydration, and who is w nourished. Neurological symptoms and pyrexia make diagnosis even more probable. There is probably a fu damental difference in the response to severe diarrh of well-nourished children to that seen in infants suff ing from protein malnutrition. *J. H. Walter*

Tworek, R. & Serokowa, Danuta, with the techni assistance of Barbara Kreska. Próba oce przydatności odczynu opsonocytofagowego w di nostyce laboratoryjnej brucelozy. [**The Value the Opsonocytophagic Test in the Laborato Diagnosis of Brucellosis**] *Przegląd Epidem* Warsaw. 1959, v. 13, No. 3, 263–71. [11 re English summary.

In a preliminary examination of factors affecting phagocytic index obtained with *Brucella abortus* and blood of healthy persons, the values obtained did differ significantly when different strains in the sa phase were used, but much higher values were obtai with rough than with smooth strains. In an examinat of the blood of 331 healthy persons a phagocytic index 0–25 was found in 256 of 288 who did not pos *Brucella* agglutinins, and in 23 of 43 who possessed agg tinins in titres up to 400. There was a statistically sig ficant correlation between the presence of agglutinins a high values of the phagocytic index. A moderat raised phagocytic index was found in 9 persons suffer from chronic brucellosis. *D. J. Baue*

Nhonoli, A. M. **Cutaneous Anthrax in Moshi D trict.** *East. African Med. J.* 1960, Jan., v. No. 1, 37–43, 4 graphs. [14 refs.]

In this fascinating paper the author records his exp ence of 101 cases of cutaneous anthrax personally trea in a 2-year period, 1957–58, in the Moshi district Tanganyika. [This concentration of clinical experie must be unique.]

The incidence of human anthrax in this region sh marked seasonal variation and appears to be dire

ated to rainfall. It rises steeply at the time of onset of e light rains in September and October, continues high ile they persist and falls abruptly with the onset of t, dry weather in February-March. The heavy rains April-June are not accompanied by a further outburst, wever. This relationship is thus explained by the thor. Anthrax spores exist in the soil and are disseminted by the wind. When young grass coated with thrax-contaminated dust springs up at the onset of the ht rains cattle which feed eargerly on it become incted. They then hand on the disease to men.

The human patients observed belonged to the Chagga be, a meat-eating people who grow coffee but who pear to import illicit and uninspected cattle from dist, anthrax-infected areas. The sexes were equally presented, the youngest patient was aged 5 months, the dest 40 years, the majority being between 10 and 30 ars of age. The commonest site of infection was on the ad (67%), in the remainder the lesion occurred at idely varying sites on the body or limbs.

The incubation period could be estimated in only 12 stances in which it ranged from 2 days to 2 weeks, with average of 4·3 days. The mode of infection proposed the author is interesting since he was able to exclude e possibilty of direct contact with animals or hides in e majority of the patients. He considers that infection the majority was acquired by eating infected meat d noted that most patients gave a history of the rapid ath of a relative who had eaten the same meat and bsequently developed acute diarrhoea. The cutaneous sions are considered to be the manifestation of a low-ade systemic infection to which, however, the elderly debilitated succumb from an alimentary localization f the infection. Further research on this aspect of the isease is indicated.

The disease began with fever and headache, followed 2 days by the appearance of an irritating though painss papule. Local oedema, a central black eschar surounded by vesicles and regional adenitis quickly deveped. A palpable degree of splenomegaly was found in 0% of the patients. *Bacillus anthracis* was found in irect smears from vesicles in 88%. 3 deaths occurred mong the 101 patients, one from anthrax meningitis and who were received in a moribund condition with large sions.

The author prefers penicillin to streptomycin as the ain therapeutic weapon, and followed-up antibiotic eatment with a short course of neoarsphenamine. He jected procaine penicillin 400,000 units daily for 3 days fter which he gave 3 daily intravenous injections of 0·3 m. neoarsphenamine. The average stay in hospital was nly 6·5 days. He concludes that cutaneous anthrax is very mild disease in Moshi. *J. H. Walters*

Albrink, W. S., Brooks, S. M., Biron, R. E. & Kopel, M. **Human Inhalation Anthrax. A Report of Three Fatal Cases.** *Amer. J. Path.* 1960, Apr., v. 36, No. 4, 457–71, 12 coloured figs. on 2 pls. [21 refs.]

Within a period of 10 weeks, 3 mill workers in Manchester, New Hampshire, died of disseminated *Bacillus anthracis* infection, and 4 non-fatal cases of cutaneous anthrax occurred. In the fatal cases there had been general symptoms of fever, beginning insidiously, increasing over 3 or 4 days, and culminating in a rapid onset of prostration shortly before death. It was only in the terminal stage that the patients were sent to hospital; one in shock, with stridor and atrial fibrillation, one in coma, with a bloody cerebrospinal fluid which was not cultured, and one with dyspnoea and cyanosis.

Necropsy reports are given in full. In 2 patients there was massive haemorrhagic mediastinitis, and in one of these, and in the third patient, there was haemorrhagic meningitis. There were the usual lesions of disseminated anthrax, but there was no tracheal or bronchial ulceration, and no pneumonia. Thus the portal of entry was not established, but it was thought to be through the respiratory tract because of the resemblance to experimental respiratory anthrax. The epidemiology is to be presented in a separate paper. *Alan B. Raper*

Parnas, I. K., Zazuga, K. & Dambrovski, T. **Studies on Water Fever in Poland (1955–1957).** *J. Microbiol., Epidemiol. & Immunobiol.* London. 1959, v. 30, No. 3, 97–105. [Translated from Russian.]

Dalrymple-Champneys, Weldon. *Brucella* **Infection and Undulant Fever in Man.**

This book was reviewed on p. 527.

VIRUS INFECTIONS

The order in this section is:—*General; Psittacosis-Lymphogranuloma group; Pox group; Respiratory group; Reovirus group; Enteric group; Arthropod-borne group; Others.*

Olivo, R. & Fabio, U. Ricerche sulla diffusione dell' infezione ornitosica nel modenese. [**Investigations on the Distribution of Ornithosis Virus in Modena**] *Giorn. di Batteriol., Virol. ed Immunol.* 1959, July–Oct., v. 52, Nos. 7/10, 313–19. [19 refs.] English summary (7 lines).

The sera of 299 healthy residents of Modena, Italy, were examined for the presence of complement-fixing antibody to ornithosis virus. Positive results in titres of 4–64 were obtained with 88 sera (29·43%), and were more frequently encountered in residents of Modena province (69 of 216, 31·9%), than in persons living in the town of Modena (19 of 83, 22·8%).

The results suggest that ornithosis virus is widely distributed among the population of the area studied.
D. J. Bauer

Buşilă, V. T., Alexandrescu, R. & Bacaloglu, D., with the collaboration of D. Sărăteanu & Elena Opresco-Lisievici. Aspecte clinice si morfopatologice într-o epidemie cu virus ornitozic. [**Clinical and Morphopathological Studies on an Epidemic of Ornithosis**] *Studii si Cercetari Inframicrobiol.* 1960, v. 11, No. 2, 187–94, 11 figs. (9 on 4 pls.) [19 refs.] French summary.

There were 5 cases, 1 fatal, on a duck farm.

Sărăteanu, D. & Nastac, E., with the collaboration of V. T. Buşilă & A. Alexandrescu. Studiul de laborator al unei epizootii cu virus ornitozic, urmată de aparitia unei epidemii. [**Laboratory Studies on an Epizootic of Ornithosis in Relation to an Epidemic**] *Studii si Cercetari Inframicrobiol.* 1960, v. 11, No. 2, 195–200. [11 refs.] French summary.

Johnson, R. W. P. & Nelson, A. M. **Haemorrhagic Chickenpox. Two Fatal Cases.** *Brit. Med. J.* 1960, Apr. 16, 1183–4.

The first patient was a boy aged 13 years under treatment for tuberculous meningitis with streptomycin, isoniazid and cortisone. When he developed chickenpox the rash became "extensively haemorrhagic," and haematuria, haematemesis and epistaxis ushered in a fatal issue. Necropsy was not performed. No reference is made to any blood examinations. The authors consider that the cortisone therapy was probably the cause of the severity of the chickenpox illness in this case.

The second patient was a woman aged 34 who had suffered from Hodgkin's disease for at least 3 years. This had been "satisfactorily" treated with radiotherapy. When she developed chickenpox pneumonia supervened and the rash became haemorrhagic. Post-mortem examination confirmed the presence of broncho-pneumonic consolidations with sub-pleural haemorrhages and revealed enlargement of the spleen and of abdominal and mediastinal lymph glands. No reference is made to any histological or blood examinations. The authors attribute the course of this fatal illness to the combination of lymphoma and chickenpox. *J. P. Marsden*

Brody, J. A., Karim, A. B. M. F. & Ahmed, M. K. **Field Evaluation of Dry Smallpox Vaccine and Aging Glycerinated Vaccine in East Pakistan.** *Pakistan J. of Health.* 1960, Jan., v. 9, No. 4, 204–11.

An attempt was made to compare the efficacy of lyophilized (dry) vaccine with that of traditional (wet) glycerinated vaccine; and to assess the potency of wet vaccine when kept at "room" temperature in tropical heat. 2 small villages figured in the trials: almost all the subjects involved were children under 10 years of age. It was considered that success in primary vaccinations was not, by itself, a sound criterion for potency of vaccine "a poor lymph can sometimes produce a high perc tage of takes after primary vaccination"; and that percentage of vaccinoid reactions in a previously v cinated group should be a more accurate index.

Of 129 subjects vaccinated, some with wet vacc some with dry, all previously unvaccinated had prim reactions. Of those with secondary reactions the p portions with maximal reaction after 72 hours w identical.

When a series of other subjects were re-vaccinated v "room temperature" wet lymph results suggested a I of potency by the 11th day.

[The authors admit that the methods of investigat used were crude. A valid criticism lies in the absence details of previous vaccination history and of scars those in whom the proportion of immediate to vaccin reactions was being used as an index of lymph poten *J. Pickford Marsde*

Bugbee, L. M., Like, A. A. & Stewart, R. B. **T Effects of Cortisone on Intradermally Indu Vaccinia Infection in Rabbits.** *J. Infect. I* 1960, Mar.–Apr., v. 106, No. 2, 166–73, 5 figs. refs.]

"The effects of cortisone acetate on experimental v cinia infection in rabbits were investigated. Cortiso treated and test groups of rabbits were inoculated w stock vaccinia virus and observed for changes in te perature, weight, blood sugar, total white blood cell co and differential, and symptomatology. In additi changes in gross and microscopic appearance of the of inoculation in skin, liver, spleen, and brain w investigated. Finally the amount of vaccinia virus each organ was quantitated. The results of these stu are reported and discussed.

"From the data obtained, it appears that cortisone a definite enhancing effect on vaccinia infection rabbits."

Jordan, W. S., Jr.; Badger, G. F.; Dingle, J. I Denny, F. W., Jr.; Curtiss, Constance; Oseason R.; Stevens, D. A. **A Study of Illness in a Gro of Cleveland Families. XVI. The Epidemiol of Influenza, 1948–1953** [Jordan, Badger Dingle]. *Amer. J. Hyg.* 1958, Sept., v. 68, No. 169–89, 7 figs. [19 refs.] **XVII. The Occurre of Asian Influenza** [Jordan, Denny, Badg Curtiss, Dingle, Oseasohn & Stevens]. *Ib* 190–212, 6 figs. [23 refs.]

XVI. "A longitudinal study of the epidemiology influenza in the same individuals and families has de onstrated that both influenza A′ and B infections occur throughout the 6-year period 1948–1953. Endemic occ rence of influenza was indicated by the fact that 5 to 1 of individuals developed significant increases in titer antibodies for A or B viruses during successive 6-mo intervals, although the disease was not recogni clinically.

"During influenza A' epidemics in 1950, 1951 and 1953, viruses were isolated from 7 to 12% of the individuals and from 25% of the families. In 1950, the serologic attack rate was 15%; in 1951 and 1953 it was 25%.

"In comparing families with virus in the 1950 and 1951 epidemics, there was a suggestion that those families harboring virus in 1950 were spared in 1951. No such difference was noted between the 1951 and 1953 epidemics.

"When compared to persons without documented exposure to virus, individuals in families from which virus was isolated in 1950 had less clinical influenza in 1951 and individuals in families infected in 1951 also had less influenza in 1953. The data are consistent with the fact that natural infection is followed by a partial immunity for 2 years.

"As reported by others, the median levels of antibodies for different antigens varied with age. Only adults and older children with measurable antibodies to PR8 and Lee viruses developed increases in titer of these antibodies as a result of infection with more recent A and B antigens.

"Epidemics occurred following periods during which the members of the population showed more decreases than increases in antibody titer, and were associated with the emergence of minor antigenic variants. The occurrence and recurrence of influenza A was related to chance, to a declining immunity, and to this antigenic shift."

XVII. "During the epidemic of Asian influenza in the fall of 1957, infections occurred in one or more members of 54 (90%) of a group of 60 families and in 146 (47%) of the 308 members of these families.

"The epidemic lasted 8 of the 10 weeks of a period of observation. Although 23% of the population had "influenza-like" illnesses, the proportion of total illnesses attributed to respiratory disease remained approximately the same as in previous years. The pattern of occurrence of respiratory disease was altered, however, in that the usual decline in late September and early October and the subsequent rise in November were reversed. The net result was that influenza did not increase appreciably the total number of illnesses experienced by the population in comparison with similar 10-week periods in previous years.

"The clinical manifestations of Asian influenza were similar to those observed in previous outbreaks of influenza A in this population. No significant changes in bacterial flora of the pharynx were detected during or after the epidemic.

"Virus was isolated from 41% of the family members. As measured by virus isolation, the secondary attack rate was 35%. The serologic attack rate in unvaccinated persons was 55%; the secondary serologic attack rate was 37%. The rate pattern within the family resembled that for the common respiratory diseases, being highest in the school children and lowest in the fathers.

"Virus was isolated from more than one person in 38 families. Twenty of the 38 intervals between first and second cases were longer than 5 days. The length of these intervals was not due to the interposition of subclinical infections.

"For measuring antibody response, particularly that induced by vaccine, the hemagglutination-inhibition test was more sensitive than the complement-fixation test, and measured titer increases of greater magnitude. There was a 52% reduction in incidence of influenza among a small number of individuals vaccinated more than 7 days."

SCHULTZ, I., GUNDELFINGER, B., ROSENBAUM, M., WOOLRIDGE, R. & DE BERRY, Patricia. **Comparison of Clinical Manifestations of Respiratory Illnesses due to Asian Strain Influenza, Adenovirus, and Unknown Cause.** *J. Lab. & Clin. Med.* 1960, Apr., v. 55, No. 4, 497–509, 2 figs. [28 refs.]

This is a study of 210 naval recruits treated at the U.S. Naval Training centre, Great Lakes, Illinois, in the summer of 1957. The diagnosis of influenza was established in 112, adenovirus infection in 64, and unknown infection in 34. Differences in clinical findings were observed between the influenza and adenovirus groups, sudden onset and headache being characteristic of influenza, a slower onset and sore throat of adenovirus infection. In the unknown aetiology group, symptomatology resembled that of influenza but with a higher incidence of pneumonia. *A. B. Christie*

DULL, H. B., JENSEN, K. E., RAKICH, Jennie H., COHEN, A., HENDERSON, D. A. & PIRKLE, C. I. **Monovalent Asian Influenza Vaccine. Evaluation of its Use during Two Waves of Epidemic Asian Influenza in Partly Immunized Penitentiary Population.** *J. Amer. Med. Ass.* 1960, Mar. 19, v. 172, No. 12, 1223–9, 2 figs. [12 refs.]

A monovalent vaccine containing formalin-inactivated Asian influenza virus was administered in doses of 50, 200 or 500 chick cell agglutinating (CCA) units respectively to 3 random groups of volunteers in a penitentiary population. A fourth group of volunteers was given a placebo control. Antibody rises measured by haemagglutination-inhibition were proportional to size of vaccine dose, reaching a peak within 2 weeks of vaccination and declining to low levels during the following 6 months. Outbreaks of Asian influenza occurred 6 weeks after vaccination and again 6 months later. The 2 larger doses of vaccine conferred 68% protection against febrile influenza during the first outbreak and this protective action was reduced only slightly by the time of the second outbreak. *H. G. Pereira*

JENSEN, K. E., WOODHOUR, A. F. & BAILEY, Ann. A. **Immunization with Polyvalent Influenza Vaccines.** *J. Amer. Med. Ass.* 1960, Mar. 19, v. 172, No. 12, 1230–38, 8 figs. [17 refs.]

Antibody responses and clinical reactions to 2 polyvalent influenza vaccines were investigated in groups of children and adults. The first vaccine contained 4 virus strains (A2/Asian/57, A/PR8/34, A1/PR301/54 and

B/GL/54) making up a total of 500 chick cell agglutinating (CCA) units per dose and the second contained in addition to these, strains A/Swine/31 and B/Lee/40, with a total of 1000 CCA per dose. Mild febrile reactions were observed in 13% of subjects in each vaccine group; these reactions were more frequent (about 20%) among children aged from 2 to 12 years. Antibody responses were higher in subjects given the 6-strain vaccine than in those receiving the 4-strain vaccine and this difference was particularly evident among children.

The authors suggest that the 6-strain vaccine might be expected to confer protection against new influenza virus variants. *H. G. Pereira*

MEIKLEJOHN, G. **Observations on Live Influenza Vaccine.** *J. Amer. Med. Ass.* 1960, Mar. 26, v. 172, No. 13, 1354–6, 2 figs.

A live influenza A2 vaccine received from Russia was administered intranasally to 27 young adult volunteers. None showed clinical symptoms during the 4 days following vaccination. Virus was recovered from throat washings of 3 of the 27 volunteers. Haemagglutination-inhibiting antibody rises against Asian influenza virus were detected in 9 of 14 volunteers with a titre of $< \frac{1}{8}$ in the pre-vaccination serum and in 5 of 13 volunteers with a detectable level of pre-vaccination antibody. These results were comparable to those obtained with 35 subjects given a single subcutaneous injection of an inactivated polyvalent aqueous vaccine containing 100 chick cell-agglutinating units of Asian influenza virus, except for the higher frequency of booster reactions among the group given the inactivated vaccine. *H. G. Pereira*

WILSON, J. S., GRANT, P. J., MILLER, D. L., TAYLOR, C. E. D. & MCDONALD, J. C. **Trial of Adenovirus Vaccine in Royal Air Force Recruits.** *Brit. Med. J.* 1960, Apr. 9, 1081–3. [12 refs.]

The protective effect of an adenovirus vaccine containing strains types 3, 4 and 7 was tested among recruits in a Royal Air Force station. Infection by influenza A, influenza B and adenovirus (mainly type 3) were prevalent in the study population at the time of vaccination and during the following weeks. Efficacy of the vaccine was indicated by a 40% reduction of respiratory illnesses among recruits vaccinated more than 1 week before admission to hospital. A 70% protection against adenovirus infections was estimated on the basis of virus isolation studies. *H. G. Pereira*

HARDING, H. B. & SNYDER, R. A. **The Epidemiology of Primary Atypical Pneumonia.** *Arch. Intern. Med.* 1960, Feb., v. 105, No. 2, 217–32. [57 refs.]

The discovery of new agents which produce acute respiratory disease, such as the adenoviruses and parainfluenzae viruses, has helped to clarify the picture but has not ruled out primary atypical pneumonia as a distinct disease of unknown aetiology. This useful review is based on 96 subjects admitted to hospitals and clinics in 1953–57, and in addition 23 cases where both patients a contacts were studied in 1957–58. This experience see to establish again that primary atypical pneumonia is n due to any of the common bacteria, rickettsiae, or v uses, but is a disease *sui generis*. The diagnosis at prese depends on clinical and X-ray findings of acute pne monitis, and particularly on a rising titre of cold agg tinins of Group O red cells, and of *streptococcus M* suspensions. Explosive outbreaks have occurred, spo adic cases are common, and there is apparently a su clinical form, readily found in contacts by the preser of rising titres of cold agglutinins. The sporadic fo has most often been observed in the late summer a autumn than at other times of the year, and more oft in females than in males. Recent work on Eaton's vi has renewed interest in this organism as a possible cau of primary atypical pneumonia. Treatment with chl tetracycline has for some years been held to be curati but this has not been confirmed in controlled studi *H. Stanley Banks*

BUKRINSKAYA, A. G. & PAKTORIS, E. A. **An Outbre of Pneumonia caused by Type 1 Haemadsorpti Virus.** *Acta Virologica.* Prague. 1960, May, v. No. 3, 184–6, 3 figs. on pl.

More than 100 children were affected in a town the Russian U.S.S.R.

CHANOCK, R. M., COOK, M. K., FOX, H. H., PARRO R. H. & HUEBNER, R. J. **Serologic Evidence Infection with Eaton Agent in Lower Respirato Illness in Childhood.** *New England J. of M* 1960, Mar. 31, v. 262, No. 13, 648–54. [16 refs.]

Serological tests for infection by Eaton virus w performed with acute and convalescent sera from childr admitted to hospital with lower respiratory tract illn or with conditions not related to respiratory infectio The sera were tested by the indirect fluorescent antibo technique by using, as antigen, lung sections from ch embryos infected with the Eaton virus. Antibody ri were detected in 18 (16·4%) of 110 children with undia nosed lower respiratory illnesses, in 1 (2·4%) of 42 ch dren with lower respiratory illnesses associated w infection by influenza, para-influenza or adenovirus, a in none of 64 children without respiratory infectio Illnesses associated with Eaton antibody rises occur endemically during all seasons of the year and were n acquired at hospital.

[See also COOK *et al.*, this *Bulletin*, 1960, v. 676.] *H. G. Pereira*

MÜLLER, H. Über die Zunahme der Sterblichkeit dritten Lebensmonat in Deutschland. [**The Caus of the Increased Mortality among 3-Month O Infants in Germany**] *Deut. med. Woch.* 19 Dec. 25, v. 84, No. 52, 2331–3, 2352, 6 figs.

The infant mortality figures for the German Fede Republic for 1952–54 show that there is a rise in mort ity in the 3rd month of life, which does not occur

reat Britain, France, Sweden or the United States; a milar rise at 3 months also occurs in the curve of mor- lity among illegitimate infants over the period 1951–56. he annual number of deaths among infants occurring the author's hospital in Bielefeld, Germany, between 950 and 1956 showed a similar rise at 3 months; when e deaths due to interstitial plasma cell pneumonia were ubtracted, however, the rise disappeared and the curve sumed the normal form. It is therefore considered at the increased mortality at 3 months observed in est Germany is due to plasma cell pneumonia, the incu- ation period and course of which is such as to lead to eath in the 3rd month of life. The absence of the rise mortality in other countries can be explained by the rity of the disease outside Germany. *D. J. Bauer*

ROUHET, Victoria, with the technical collaboration of H. GOAREGUER. Infections à virus entériques chez les enfants et syndromes cliniques associés. [**Enteroviruses Infections and Associated Clinical Symptoms in Children**] *Ann. Inst. Pasteur.* 1960, Apr., v. 98, No. 4, 562–8.

During the year 1958–59 faecal samples from 202 chil- ren suspected of having poliomyelitis were examined. 06 viruses were isolated in monkey kidney cells (77 oliovirus, 14 ECHO, 7 Coxsackie B, 5 adenovirus and 3 nidentified agents). ECHO 3, 7, 9, 11, 14 and Cox- ackie B1 and B5 were isolated from cases of meningitis. oxsackie B3 and 5 and ECHO 1, 6, 7 and 12 were iso- ted from patients with paralysis, ataxia or encephalitis. he patient with encephalitis developed antibodies to CHO 6 virus during infection. Antibody rises to the fecting virus were also noted in a patient with ataxic ymptoms (ECHO 7) and 2 with paralysis (Coxsackie B5 nd ECHO 6). Another patient with ataxia yielded CHO 1 and had antibodies to this virus in the acute rum sample but no antibodies to any type of polio- irus. It is possible that these enteroviruses may have layed an aetiological role in the children's illnesses.

A. J. Beale

HOGBEN, G. H. & YARROW, A. **Poliomyelitis in a Day Nursery and the Use of Gamma Globulin.** *Med. Officer.* 1960, Mar. 11, v. 103, No. 11, 147–8.

In a day nursery having 65 children in attendance 2 ases of paralytic poliomyelitis occurred within a period f 14 days in unimmunized children. Virus studies howed that 17 of the remaining children and 3 out of 8 staff were excreting poliovirus type 1. Since 30 of the hildren had had only 1 or no injection of poliomyelitis accine, it was decided to offer gamma globulin to this roup as a prophylactic, 5 ml. (0·5 gm.) if under 1 year f age and 10 ml. (1·0 gm.) if over that age.

The result was inconclusive, but those given gamma lobulin excreted the virus for a shorter period of time han those who were not given gamma globulin. Although it is considered too late to give gamma globu- in to *household* contacts when a clinical case occurs, the uthors suggest that spread in a day nursery may be lower than in a household. They would be inclined, as a result of this experience, to try the effect of giving gamma globulin in a day nursery immediately after the occurrence of the first case. *H. Stanley Banks*

ULSTRUP, J. C. & MEMMER, R. **Prevalence of Poliomyelitis neutralizing Antibodies in Norwegian School Children before Vaccination.** *Arch. f.d. gesamte Virusforschung.* 1959, v. 9, No. 3, 348–59, 6 figs. [10 refs.]

A survey of poliovirus neutralizing antibodies among Norwegian school children in the 6th and 7th elementary classes (mainly 12–13 years old) was made in October 1956. 3,453 children were bled and the sera tested against all 3 types of poliovirus. The overall percentage of triple negatives was 3·6% but great differences were found in different parts of the country in the incidence of antibodies to individual types or to combinations of types. In general, towns in the north and west parts of the country had a higher incidence of antibodies than those in the southern and eastern parts. In the 3 previous years the incidence of paralytic poliomyelitis had been 80 per 100,000 in the north-west and 30 in the south-east. The observation that triple positives and negatives are more frequent than would be expected if the viruses spread independently was confirmed [MELEN *et al.*, this *Bulletin*, 1959, v. 34, 523]. This may be explained partially by shared antigens or by the fact that conditions leading to the acquisition (or failure) of one type of antibody will also act for the other types.

In this survey the colour test devised by SALK *et al.* [*ibid.*, 1955, v. 30, 184] was used with HeLa cells, and is described in detail. As used it was found to be more sensitive in detecting antibodies than the conventional method with human amnion roller tube cultures and observation of the absence of antibodies in inhibition of the cytopathic effect. With a 1/5 dilution of serum as the criterion of a negative colour test then the agreement between the 2 methods of assay in determining the presence or absence of antibodies was close. *A. J. Beale*

MAASS, G., JANIK, F. & HERTENSTEIN, C. Virologische Umgebungsuntersuchungen während einer Poliomyelitis-Epidemie in einem Kinderheim. Die Ergebnisse im Verlauf der Epidemie und ihre Bedeutung für seuchenhygienische Massnahmen. [**Virological Studies during a Poliomyelitis Epidemic in a Children's Home: Results in the Course of the Epidemic and their bearing on Hygienic Measures.** *Deut. med. Woch.* 1959, Nov. 6, v. 84, No. 45, 2026–30, 2060, 5 figs. [30 refs.]

The authors have made continuous virological observations during the course of an epidemic of poliomyelitis which occurred in a children's home in Germany in 1958–59, occupied by 51 children aged 3–7 years with a staff of 16. The first case occurred in a child aged 5 who developed typical paralytic poliomyelitis with subsequent recovery. The second case was mild, with transient facial palsy, and more detailed clinical information was not

available. Within 2 weeks of the 1st case 4 of 10 children who lived in the same room developed short-lasting pyrexia, which was regarded as an abortive attack. Poliomyelitis virus was isolated from the stools of 38 (77%) of 49 children who were in contact with the 2 patients with paralytic illness; the virus was of type 1 in 35 and type 3 in 3 instances, and continued to be excreted in the stools for up to 11 weeks in a few cases. Type 1 virus was found in the stools of 1 member of the staff. Type 1 neutralizing antibody was found in the sera of all the children 3 weeks after the occurrence of the first cases, but types 2 and 3 antibodies were absent in most cases; there was little change in the titres in a second investigation carried out after 8 weeks. Type 1 complement-fixing antibody could be found in 17 of 30 (57%) children who excreted type 1 virus. *D. J. Bauer*

FENDALL, N. R. E. **Poliomyelitis in Kenya. A Review of the Present Position.** *East African Med. J.* 1960, Feb., v. 37, No. 2, 89–103, 2 figs. & 2 graphs. [26 refs.]

The number of reported cases of poliomyelitis in Kenya has been rising since 1944. There have been 2 severe epidemics in 1954 and 1957. The attack rates for Europeans, Asians and Africans in the 1954 outbreak were 244, 40 and 4·6 per 100,000 respectively. The brunt of the disease was borne by children under 5 years although substantial numbers of cases occur in older Europeans. A review of the advantages and disadvantages of killed and attenuated vaccines is presented. It was decided that attenuated vaccine should be used mainly on the grounds that it produced antibodies more quickly which might last longer, was easier to administer and cheaper to buy. A severe outbreak of type 1 poliomyelitis developed at the end of 1959, so a vaccination programme was started with attenuated vaccine [presumably type 1]. An isolated district, Kerugoya, was chosen for the experiment and 60,000 children were vaccinated. During the preceding 7 weeks 23 cases occurred in this area and in the following 7 weeks 16 cases occurred. 11 of these patients had received vaccine. It was thought that these patients were probably incubating the disease when vaccinated or that too little time had elapsed for immunity to develop.

[One of the defects of killed vaccine is stated to be its ineffectiveness against non-paralytic poliomyelitis. This ineffectiveness has been shown to be due to the fact that the majority of cases of "non-paralytic poliomyelitis" are not due to poliovirus. The isolation of poliovirus from vaccinated cases of paralytic or non-paralytic "poliomyelitis" is much reduced [see LENNETTE *et al.*, this *Bulletin*, 1960, v. 35, 479]. The 11 vaccinated patients who developed paralysis did so 1, 6, 8, 10, 12, 14 (2), 15, 17, 20 and 34 days after vaccination. The results of virus studies on these patients are not reported. It is to be hoped that they will be later. Another approach to the problem of preventing poliomyelitis in populations emerging into epidemic susceptibility is described in an article by MELNICK abstracted below.]

A. J. Beale

MELNICK, J. L. **Studies on the Serological Epidem logy of Poliomyelitis as an Index of Immuni in certain Caribbean Islands, British Guian and Ecuador.** *West Indian Med. J.* 1959, De v. 8, No. 4, 275–98, 1 map & 17 figs. [10 refs.]

The results of a serological survey for antibodies the three types of poliovirus in the Caribbean (Antig Barbados, Haiti, British Guiana in 1957 and Trinidad 1954) and Ecuador are described. It was found that all the communities there was a rapid rate of acquisiti of antibodies similar to that found among lower ec nomic groups in the U.S.A. in 1951-53. The antibo titre tended to fall with increasing age though the prop tion with levels above 1/10 remained high. The stud showed that the susceptibles were mainly under 5 a this is borne out by the concentration of poliomyelitis this age-group. However, the inverse correlation betwe infant mortality and poliomyelitis epidemics noted PAYNE at the Third International Polio Conference, 19 [this *Bulletin*, 1956, v. 31, 1196], was not universal these studies. Thus Antigua has had no epidemic desp an infant mortality rate between 70 and 90 for most the past 10 years, whereas both Trinidad and Barbad have experienced epidemics despite very high infant m tality rates. At present most of these populations do n have a serious poliomyelitis problem, but experience the U.S.A. where severe outbreaks have started to occ in lower socio-economic districts, *e.g.* in Detroit (19 and Des Moines (1959), suggests that the breathing sp may be short. It is suggested that a serological monit ing system be set up in such areas so that poliovaccin tion can be administered when susceptibles start accumulate and that expensive vaccine is only given population groups actually in need of protection.

[In such a monitoring system the proper representat collection of sera is most important—it is unfortun that in this report rather little is said about the collecti of sera. In his previous publications the author H usually given precise details of the sampling metho employed. This is a most interesting paper which commended to the attention of health officials faced w the difficult problem of how to counter the threat emerging poliomyelitis epidemics with limited resource *A. J. Beale*

HORSTMANN, Dorothy M., SAENZ, A. C. & OPTON, E. **Immunity to Poliomyelitis in Guatemala. Serological and Virological Survey.** *Bull. Wo Health Organization.* Geneva. 1960, v. 22, N 3/4, 255–62, 6 figs. [11 refs.]

A survey of the immune status and prevalence enteroviruses in Guatemala is described. It was fou that most cases of poliomyelitis were in children unde years of age and during the first 4 years of life m majority of children underwent a primary infection w poliovirus. Thus protection is required early in li Studies made on 36 children aged 3 to 6 years show that up to 3 doses of Salk vaccine made little differen to the antibody titre of children of this age in this ar This was partly because virtually all children acqui

tibodies as a result of natural poliovirus infection any- y. About one-third of the children aged 5 months to years were excreting an enterovirus and 10% a polio- us. This fact makes the choice of a poliovaccine for ch areas extremely difficult. An oral vaccine is attrac- e because of its convenience and modest cost but these e the conditions where it is probably least effective cause of viral interference [see LEBRUN *et al.*, p. 794.]

A. J. Beale

NGNER, I. & JUNGNER, G. **Creatinine and Creatine Clearance in the Acute Stage of Paralytic Poliomyelitis.** *Acta Med. Scandinavica.* 1960, Apr. 20, v. 166, No. 5, 357–68, 1 fig. [25 refs.]

"An investigation in 8 cases of severe poliomyelitis s shown that the non-protein nitrogen (NPN) in the ood may be moderately raised, without a coincident ange in serum creatinine or endogenous creatinine clear- ce. Since the serum creatinine level falls steadily in ralytic poliomyelitis, this test as well cannot be regarded a suitable sign of failing renal function. Strong indi- tions exist for using the endogenous creatinine clearance tead to evaluate renal function in acute poliomyelitis.

"Determinations of creatinine and creatine clearance ve shown a considerable decrease in the reabsorption creatinine in the renal tubules during the acute stage severe poliomyelitis. The creatine excretion shows h great variability in each individual, as well as from se to case, that it does not reflect the muscle destruc- n other than qualitatively."

NGNER, G. & JUNGNER, I. **Transaminase Activity in the Serum in Acute Poliomyelitis.** *Acta Med. Scandinavica.* 1960, Apr. 20, v. 166, No. 5, 369–78, 2 figs. [35 refs.]

"The activity in the serum of glutamic oxalacetic nsaminase (GOT) and glutamic pyruvic transaminase PT) has been followed by repeated determinations ring the acute stage in 17 cases of paralytic poliomye- is. Two completely paralyzed patients are found to ve raised transaminase values, with peaks up to 100– 0 Karmen units. In cases of severe paralysis, the tivity generally remains within normal limits, but dur- g short periods values of 50–100 units were recorded. cases of mild and moderate paralysis, the activity is nsistently normal.

"The rise in GPT is found to be relatively greater an that in GOT, and in three cases investigated a rise ornithine carbamyl transferase (OCT) activity in the rum could also be demonstrated. This is interpreted evidence that the increases in enzyme activity are due liver damage. Like other neurogenic myopathies, polio- yelitis does not, in itself, produce a pathological rise serum transaminase.

"The influence of artificial respiration, failing cardiac nction and a direct virus attack on the liver are dis- ssed as causes of the liver damage. The results of the vestigation indicate that a disturbance in liver function the form of asymptomatic hepatitis, possibly combined th overloading of the liver owing to the increased work implied by the great muscle destruction, is fairly common in paralytic poliomyelitis. It is recommended that the risk of such sub-clinical liver involvement should be taken into account in the management of poliomyelitis patients."

KOKKO, U. P. & MURRAY, R. **Human and Animal Antibody Responses to Commercial Poliomyelitis Vaccine.** *Bull. World Health Organization.* Geneva. 1960, v. 22, Nos. 3/4, 263–72, 2 figs.

Serum samples were obtained from 245 infants aged 6–44 months, originally without antibodies to all 3 types of poliovirus, before and 1 month after 2 doses of commercial killed poliovaccine made in the U.S.A. 182 infants were bled before and 1 month after a third dose given 6 to 7 months after the second. After 2 doses 50%, 94% and 46% acquired antibodies to types 1, 2 and 3 respectively. After 3 doses the figures were 89%, 98% and 88% at a titre of 1 in 4 or greater. When tested at 1 in 16 the figures were 75%, 97% and 68%. Attempts were made to compare the performance of 6 vaccines in man and in animal potency tests. The correlations were very imperfect although they gave some rough indication of potency. The results given for chick potency tests seem slightly better than for monkey tests. One vaccine (D) seemed best in children but was one from the bottom in the monkey potency test in respect of type 1.

[These results show that 3 doses of average killed poliovaccine give an immune response in the great majority of triple negative infants. The titres are, however, very low and booster doses are almost certainly required for a durable immunity. It is also apparent that better methods of testing potency are required.] *A. J. Beale*

ULSTRUP, J. C. & MEMMER, Ramona. **Antibody Response to Salk Vaccine in Norwegian School Children.** *Arch. f.d. gesamte Virusforschung.* 1959, v. 9, No. 3, 343–7, 5 figs.

The response of Norwegian school children (6th and 7th elementary classes) to Salk type poliovaccine (of American and Danish manufacture) is presented. The children received 0·1—0·2 ml. of poliovaccine intracutaneously. The first 2 doses were given a month apart and the 3rd 6 months after the 2nd. 872 children were bled 1 month after the 2nd dose and 693 after the 3rd. Both specimens were obtained from 473 children. The sera were titrated for antibodies by means of a *p*H inhibition technique with HeLa cells. 1000 *p*H-D_{50} of virus were used and virus serum mixtures were held at room temperature for 1 hour before the addition of cells. The response of triple negative children was poor, under 50% making an antibody response to the type 1 or 3 component to 3 doses of vaccine. The response to type 3 was much better, 32 out of 33 responding to 3 doses. The presence of heterotypic antibody greatly improved the results. Of children with type 2 antibodies, 34 out of 36 responded to type 1 and 30 out of 36 to type 3. The presence of type 1 or 3 heterotypic antibodies enhanced the response to these 2 types to a lesser degree. While a

third dose boosted the geometric mean antibody titre to type 2 markedly and to type 3 slightly, it appeared to have no effect for type 1. These vaccinations were started in October 1956. Since then 1 ml. by the subcutaneous route has been substituted.

[These poor responses may be partially explicable by the small intracutaneous dose and by the large challenge dose of virus and the short period of neutralization compared with British Medical Research Council practice, see this *Bulletin*, 1957, v. 32, 510.]

A. J. Beale

Dane, D. S. & Dick, G. W. A., with J. J. McAlister & R. T. Nelson. **Epidemic Control of Poliomyelitis with Inactive Virus Vaccines. Studies in Cynomologus Monkeys.** *Lancet.* 1960, Apr. 16, 845–9, 5 figs. [12 refs.]

Killed poliovaccine in 1 ml. dosage has not proved effective in the face of epidemic poliomyelitis [Poos and Nathanson, this *Bulletin*, 1957, v. 32, 13, and Bundesen *et al.*, *Ibid.* 831]. However, when 10 ml. of vaccine is given the antibody response to 1 dose is greatly improved [Baron *et al.*, *Ibid.*, 1959, v. 34, 991, Barnett and Baron, *Ibid.*, 1960, v. 35, 585]. In the present work cynomolgus monkeys were given a single 10 ml. dose of standard commercial vaccine (giving an antigen extinction titre in guineapigs of $10^{-1.2}$) and 7 days later were challenged with type 1 poliovirus (Barr strain) intracardially. 9 of 11 control monkeys given tissue culture fluid had severe central nervous infection with poliovirus. 4 of the 11 vaccinated animals became paralysed. These were the 3 animals failing to produce antibodies and 1 that had a titre of 1 in 4. The remaining 7 vaccinated animals which were not paralysed showed low titres of antibody 1 week after vaccination which had disappeared 7 weeks later except in 1 animal which showed a rise in titre presumably due to a subclinical infection. All the paralysed animals tested had viraemia and also virus in their throat. Virus was only irregularly found in the faeces. It was thought possible that the virus multiplied first in the throat and then spread to the blood although virus was rarely found in throat swabs before viraemia occurred. However, this was thought to be due to a much less sensitive technique for the detection of virus in the throat compared with in the blood. The results suggest that one 10 ml. dose of killed vaccine might be effective in the face of epidemic poliomyelitis in man. *A. J. Beale*

Martins Da Silva, M., Lopez Berrios, M. & Alcocer, J. J. Vacunación con virus poliomielítico atenuado en un área epidémica—Managua, Nicaragua, 1958. [**Vaccination with Attenuated Poliomyelitis Virus in 1958 in Managua, Nicaragua, an Epidemic Area**] *Bol. Oficina Sanitaria Panamericana.* 1959, Sept., v. 47, No. 3, 201–13, 5 figs.

In May–October 1958 an outbreak of type 2 poliomyelitis occurred in Nicaragua, with 254 recorded cases among a total population of 1,377,599 (18·4 per 100,000); 107 cases occurred in the department of Managua, and 86·8% of the total number were in children younger than 3 years. 80% of the children in Managua aged 2 mon to 10 years (a total of 42,199) were given live attenua poliomyelitis vaccine of type 2, followed later by administration of type 3 and finally type 1. By following summer the number of children who had b given type 2 vaccine had risen to 59,855. The vaccina campaign was well received by the population, apart fr some opposition from the press and broadcasting vices. Examination of sera taken from 505 child before the administration of type 2 vaccine showed only 8% did not possess type 2 neutralizing antibo Sera were obtained from 242 of these children a vaccination, and neutralization tests showed that 90 122 (74%) originally lacking antibody responded to va nation, including 39 of 53 (74%) to type 1, 11 of (58%) to type 2 and 40 of 50 (80%) to type 3. A from 4 cases of urticaria no side-effects were observe a result of vaccination. *D. J. Baue*

Van Rooyen, C. E. & Ozere, R. L. **The Pres Status of Oral Vaccination against Poliomyel and Future Problems.** *Canadian Med. Ass.* 1960, Apr. 9, v. 82, No. 15, 759–66. [81 refs.]

This is a very complete review of the present posi of attenuated poliovaccines. The need for more rese before the mass use of attenuated strains in a country Canada is stressed. Genetic stability, antigenicity avirulence under normal conditions in countries enjo a high standard of living and in non-tropical areas require more study. The probable future method of c trol of poliomyelitis is thought to be by displacemen the wild poliovirus reservoir by attenuated strains. order to achieve this on a long term basis strains m not be too avirulent to be able to maintain themse in the community. *A. J. Bea*

Lebrun, A.; Cerf, J.; Gelfand, H. M.; Courtois, Plotkin, S. A.; Koprowski, H. **Vaccination w the CHAT Strain of Type 1 Attenuated Po myelitis Virus in Léopoldville, Belgian Cor 1. Description of the City, its History of Po myelitis, and the Plan of the Vaccina Campaign** [Lebrun, Cerf, Gelfand, Court Plotkin & Koprowski]. *Bull. World He Organization.* Geneva. 1960, v. 22, Nos. 3/4, 2 13, 2 figs. **2. Studies of the Safety and Effic of Vaccination** [Plotkin, Lebrun & Koprow *Ibid.*, 215–34, 7 figs. [20 refs.]

These 2 valuable papers give a very complete acc of the use of the attenuated CHAT type 1 strain of p virus in Léopoldville [population 350,000] in the Bel Congo during the late summer and autumn of 1958.

The first paper fills in the background. Since 1 there appears to have been an increase in the incid of paralytic poliomyelitis. The exact rate has fluctu from year to year but the average in the period 195 1958 was 18·8 per 100,000 of the population for Afri and 31 for Europeans. Among the African popula almost all the paralytic poliomyelitis occurred in chil under 5 years of age. A serological survey showed

the age of 5 years 90% of the children had antibodies each of the types of poliovirus but below 3 years substantial numbers of children were without antibodies to e or another type and under 1 year 74% of the children re triple negatives. It was therefore decided to protect e African population against poliomyelitis, concentrating the campaign upon children under 5 years of age. It as decided to use living virus vaccine for the following asons: (1) oral administration is much easier; (2) satisctory experience with yellow fever vaccination suggested at 1 dose should be sufficient to last a lifetime; (3) it as easy to use in infants of about 6 months; (4) it was eaper than killed vaccine. The CHAT strain of attenued poliovirus was therefore used. $10^{5.0}$ TCD50 was the ual dose but children under 30 days received $10^{6.2}$ CD50. Vaccine was given in a 1 ml. dose by means of automatic syringe squirting the virus into the back of e throat. The vaccination campaign began in August 58 and has continued ever since.

The results of the vaccination campaign are given in e second paper. Up to April 30th, 1959, nearly 46,000 ildren were vaccinated out of a population of 76,000. early 22,000 were estimated, on the basis of a sample rological survey, to be without type 1 antibodies and ,000 to be without antibodies to all 3 types of polio- rus. Follow-up examinations were carried out on about 00 children and showed that after vaccination the incince of reported minor illnesses was increased but there as no evidence that any serious disease due to the ccine strains was caused. However, about 2 months ter vaccination an epidemic of type 1 paralytic polioyelitis occurred and in the next few months there were cases of paralytic poliomyelitis in Léopoldville. Of ese 99 patients, 89 were unvaccinated and 10 had reived the CHAT strain of poliovirus. 7 were vaccinated ore than 2 months previously, one 20 days before, one 1 2 days before and one 6 days before, but he was probly incubating the disease at the time of vaccination. he epidemic was not thought to be induced by the HAT strain because it started in unvaccinated persons ho had had no known contact with vaccinated children nd also because the character of the virus isolated from atients whether vaccinated or not differed in several imortant characters both from the original CHAT strain nd also from the strain of virus isolated from persons d the CHAT strain [see KOPROWSKI *et al.*, p. 822]. 340 hildren vaccinated between August and November 958 who were found to be without type 1 antibodies ere bled again 3 months later. Similarly 62 nonaccinated children were bled in October 1958 and e-bled in January 1959. It was found that 60% f the 340 vaccinated persons had acquired antiodies to type 1 poliovirus and that 35% of the 62 nonaccinated subjects had done so. Antibodies to types 2 nd 3 had been acquired by 7% of the small number of hildren who lacked antibodies to these types of polioirus. The relatively low conversion rate was ascribed o interference by other viruses known to be circulating n the area [see VANDEPUTTE, this *Bulletin*, 1960, v. 35, 78]. Efforts were made to assess the effectiveness f the vaccine with 2 methods. The first was based pon calculating the attack rate in terms of 100,000 erson/weeks of exposure and by this method it was estimated that the vaccine was about 60% effective. (In a footnote the authors say that in the additional period from 1st May to 30th September 1959 there were 32 additional cases, 10 in vaccinated and 21 in non-vaccinated persons [1 child seems to have been lost], and because of the greatly increased number of vaccinated children this has increased the estimated protection by the person/time method to 66%.) The second method, suggested by Dr. GARD [see p. 823] was to calculate the risk of contracting paralytic poliomyelitis for each week of the epidemic and then calculating to see whether the expected number of cases occurred in the vaccinated children. It was found that there were significantly fewer cases than would have been expected in the vaccinated children.

[The type 1 conversion rate of 60% is a maximum figure. Some of the children may have acquired antibodies from a wild poliovirus infection rather than the vaccine since type 1 poliovirus was epidemic at the time and 35% of the control children acquired antibodies. Some of these control children could have been infected with attenuated virus by contact with the vaccinated children.] *A. J. Beale*

KRAUS, N. & ADAM, J. Coxsackie-Infektion im Sommer und Herbst 1958. **[Coxsackie Infection in Summer and Autumn 1958]** *Ztschr. f. ärztl. Fortbildung.* 1959, Nov. 25, v. 53, No. 22, Pt. 2, 1409–13, 1 fig. [52 refs.]

In the summer and autumn of 1958 an epidemic of Coxsackie infection occurred (presumably in the Timisoara area of Rumania), during which the authors observed 98 patients who were treated in hospital; 44 were suffering from herpangina, 21 from meningitis, 8 from non-paralytic poliomyelitis, 3 from abacterial enteritis, 14 from nephritis, 2 from parotitis and 6 from epidemic myalgia with meningitis. From the stools, nasopharyngeal washings or cerebrospinal fluid of 35% of the patients a virus could be isolated which was identified as Coxsackie A type 10, and high titres of type 10 neutralizing antibody were found in the patients' sera. The clinical aspects of the various forms of the disease are described in detail. The nephrotic form was characterized by pains resembling those of pyelocystitis with protein, red cells and granular casts in the urine, but without oedema or hypertension. The meningitic form of the disease predominated in May-August, and was then replaced by herpangina. *D. J. Bauer*

HSIUNG, G. D. **Studies on Variation in Coxsackie A-9 Virus.** *J. Immunology.* 1960, Mar., v. 84, No. 3, 285–91, 3 figs. [13 refs.]

Coxsackie A 9 can be adapted to grow in Patus monkey kidney cells by prior passage in these cells which have been irradiated [this *Bulletin*, 1958, v. 33, 715; 1959, v. 34, 955]. It then produces small plaques and is relatively avirulent for suckling mice. One passage in suckling mice or rhesus monkey kidney cells results in a great increase in the large plaque size mouse-virulent type virus which will not grow on unirradiated Patus kidney

cells. The small plaque variant was shown in single cycle experiments to grow much more slowly than the large plaque type. The large plaque type could be selected by the rhesus monkey kidney cells but because large numbers of large plaque forms appear after 1 passage of a pure clone of small plaque type in these cells it is thought that a host-controlled variation of the type described by Luria and Human for bacterial viruses may be operative [*Ibid.*, 1953, v. 28, 853]. *A. J. Beale*

Neeb, H., De Haas, R. A., Verlinde, J. D., Van Tongeren, H. A. E. & Wilterdink, J. B. "Biakkoorts", een $ECHO_6$-virusinfectie. [**Biak Fever, an ECHO 6 Virus Infection**] *Nederl. Tijdschr. v. Geneesk.* 1959, Nov. 21, v. 103, No. 47, 2361–4, 1 fig. English summary (6 lines).

In September 1958 an outbreak of a new type of infectious disease, subsequently called Biak fever, occurred in Biak and other parts of Netherlands New Guinea. The disease was apparently introduced by air communications and the first cases occurred among employees of the KLM airline. During the next 2 months the disease gradually spread to other localities, giving rise to outbreaks which lasted for 1½ to 2 months with an incidence of 10–20%. About 120 patients received medical aid in Biak, and about 300 in each of 3 other localities. The disease was characterized by severe frontal headache, pain in the neck, fever of 2–5 days duration, relative bradycardia, anorexia and Kernig's sign. The cerebrospinal fluid showed pleocytosis and was under increased pressure. A transient morbilliform exanthem was seen in 6 cases. The illness lasted up to 7 days and the outcome was favourable in all cases; the probable incubation period was 2–4 days. Investigation of paired sera from patients in neutralization tests with reference strains of virus indicated that the outbreak was due to infection with an ECHO virus of type 6.

[The same outbreak is reported by the authors in *Trop. and Geograph. Med.*, Amsterdam, 1959, v. 11, 276.] *D. J. Bauer*

Jakob, A. Hepatitis epidemica und Schwangerschaft. [**Epidemic Hepatitis and Pregnancy**] *Ztschr. f. ärztl. Fortbildung.* 1960, Mar. 1, v. 54, No. 5, 247–50.

The observations described in this paper were made in 10 cases of epidemic hepatitis in pregnancy in the years 1957-59, during which period a total of over 1,000 cases of hepatitis had occurred in the Sonneberg district. The questions about which more information is needed were: (1) what is the cause of epidemic hepatitis in pregnancy? (2) can the infection be carried to the child through the placenta? (3) should the mother be permitted to suckle the child or not?

The literature bearing on these questions is quoted but the evidence is conflicting. There are case reports on the 10 cases studied by the author of this paper. The main results of the study were: (1) hepatitis in pregnancy generally takes a severe course and is particularly severe when infection occurs particularly in early p nancy. After the birth of the child the maternal hepa is cured with relative rapidity, (2) in no instance was dence obtained of spread of the infection to the in through the placenta and (3) with adequate treatmen the mother and the precautions which are detailed would appear that suckling of the child does not ca the infection. *M. E. Delafiel*

Sousek, O. & Jiránková, V. Infekční hepatitis těhotenství. [**Infectious Hepatitis and P nancy**] *Časopis Lékařů Českých.* Prague. 1 Apr. 29, v. 99, No. 18, 571–4. [16 refs.]

The English summary appended to the paper is follows:—

"1. To the department for infectious hepatitis Prague 4 during the past 7 years 263 pregnant wo were admitted. In 152 IH was confirmed. In the there were suspect abortive types of 1H, toxaemias pregnancy, biliary diseases and haemolytic jaundice. the discussion the diagnostic difficulties are briefly n tioned.

"2. Normal pregnancy of healthy women in our gr did not render the prognosis of IH any worse. All fac which interfere with the general and liver metabolism the hepatic circulation may cause a malignant co of IH.

"3. IH does not cause spontaneous abortions or mature birth of the infant any more frequently than other infection. The results of common laboratory ex inations cannot serve as a reliable guide of the da of imminent abortion or premature labour in wo with IH.

"4. Clinical signs are earlier and more reliable i cators of an incipient hepatic insufficiency in IH t laboratory tests. Hepatic insufficiency is a contraind tion for termination of pregnancy, even in IH. Term tion of pregnancy is indicated only as a preventive m sure in all instances where it is likely that the pregn would cause a deterioration of the already inadeq metabolism in women with IH or during the pe following IH."

Deutsch, J. Die Thioctsäure und ihre therapeuti Anwendung bei der Hepatitis epidemica. [**Thio Acid and its Use in the Therapy of Epide Hepatitis**] *Ztschr. f. ärztl. Fortbildung.* 1 Mar. 1, v. 54, No. 5, 251–4. [21 refs.]

The literature on thioctic acid (6, 8, Dithiocap acid)—its history, chemistry, biochemical reactions value in the treatment of a number of hepatic and o diseases—introduces an account of the author's ex ence in 38 patients with acute infective hepatitis to w the drug was given, alternating with the same nun of hepatitis patients treated by other methods.

The dosage of thioctic acid was 13·0 mgm. given in venously every third day until a total of 78·0 mgm. been given followed by a daily dose of 30·0 mgm. about a week, to a total of 180 mgm. No signifi difference was manifest between the experimental and

ntrol groups in regard to the duration of jaundice, liver largement or return to normal values of bilirubin con- ntration and the thymol test. In 5 patients in whom idence of hepatitis had persisted for a number of eks, no definite value of thioctic acid treatment could found. Nevertheless, in view of the published experi- ce of some other workers it is proposed that thioctic d therapy might be indicated in (1) cases of severe patitis to prevent hepatic coma, (2) patients who were en corticosteroids in a high dosage or over a long riod in order to prevent fatty changes in the liver, (3) tients who were being given drugs which might damage liver cells and (4) cases of protracted epidemic hepa- s. *M. E. Delafield*

HINDLER, R. & MOHR, W. Über eine Infektion mit dem Virus der Hepatitis contagiosa canis beim Menschen. [**A Case of Human Infection with the Virus of Canine Hepatitis**] *Deut. med. Woch.* 1959, Nov. 13, v. 84, No. 46, 2080–84, 2104, 1 chart. [Numerous refs.]

In complement-fixation tests with an antigen consisting an extract of the liver of a dog experimentally infected th canine hepatitis virus which were carried out in 57 on the sera of 1,398 patients in hospitals in the mburg area of West Germany, a positive result was tained in 2 instances, in 1 of which a rise in titre m 5 to 80 could be observed, indicating the possible currence of an acute infection with the virus. The um was from a 14-year-old girl, who developed a hot sh of the face and neck with itching, which spread to e arms and later to the whole body. On admission to spital there was scarlatiniform exanthem on the trunk d a semi-confluent macular exanthem on the arms, th marked conjunctivitis, slight generalized enlargement the lymph nodes with monocytosis and a temperature 38·2°C. On the 3rd day of illness canine hepatitis mplement-fixing antibody was found in a titre of 20, hich rose to a maximum of 80 on the 16th day. The mptoms gradually receded and the patient was dis- arged well on the 18th day after the onset of illness. mplement-fixing antibody was still present in a titre 10 after 5 months. *D. J. Bauer*

AQUERIZO A., L. & MÁRMOL C., Fanny. Encefalitis a virus transmitidos por artrópodos. III. Influencia de la edad de los ratones blancos en la susceptibilidad para una cepa de virus Venezolano. [**Virus Encephalitis Transmitted by Arthropods. III. Influence of the Age of White Mice on Susceptibility to a Strain of Venezuelan Equine Encephalomyelitis Virus**] *Rev. Ecuatoriana de Hig. y Med. Trop.* Guayaquil. 1958, Oct.–Dec., v. 15, No. 4, 163–76. [12 refs.] English summary. IV. Investigacion del tipo Venezolano en algunos sueros humanos en la costa ecuatoriana. [**IV. Investigation of Venezuelan antibody in Human Sera in the Coastal Region of Ecuador**] *Ibid.*, 217–24, 1 map. English summary.

An investigation has been made of the susceptibility of ice of different ages to infection with Venezuelan equine encephalomyelitis virus by the intracerebral and intraperitoneal routes. The mean survival times after infection with various doses of virus are shown in detail in numerous tables. The mean survival time of mice aged 1 week ranged from 1·0 to 2·6 days, and lay between 6 and 8 days in mice aged 6 weeks. No marked difference was observed in the LD50 titres obtained in mice of different ages. Neutralizing antibody to Venezuelan equine encephalomyelitis virus was found in the sera of 109 of 410 (26·58%) persons resident in the coastal region of Ecuador who had not experienced any known attack of the disease, and in the sera of 8 of 13 mules and 6 donkeys. *D. J. Bauer*

GROSHKOVA, I. M., PAVLOVA, M. S., POPOV, V. M. & TIUSHNAKOVA, M. K. **Data on the Epidemiology of a Focus of Tick-Borne Encephalitis in the Kustanai Oblast.** *Problems of Virology.* London. 1959, v. 4, No. 2, 67–70. [Translated from Russian.]

The first 9 cases of tick-borne encephalitis were reported from the Kustanai Oblast in 1955, 7 of them in May. All except 1 had recently come to the area from the Ukraine and were engaged in the cultivation of virgin soil. This is an area of plain relief covered with aspen-birch spinneys among which there is some cultivated land, between 52–53°N and 64–66°E. This is different from the usual habitat of *Ixodes persulcatus*, and of 2,239 ticks collected in one part of the area in 1957 97% were *Dermacentor marginatus* and 1% *D. pictus*; in another place all of 997 ticks were *D. maginatus*. 1,180 *D. marginatus* were inoculated into mice and Russian spring-summer virus was isolated from 5 pools containing 104, 33, 58, 102 and 51 ticks. 3 strains were isolated on primary inoculation, 1 after 1 blind passage and 1 after 2 blind passages. The identity of the strains was established by neutralization and complement-fixation tests. *C. E. Gordon Smith*

ZAKORKINA, T. N. [**The Virological Characteristics of a Focus of Tick-Borne Encephalitis near the Krasnoyarsk State Electric Power Plant Construction Site**] *Med. Parasit. & Parasitic Dis.* Moscow. 1959, v. 28, No. 5, 563–8. [In Russian.] English summary.

In 1957 an epidemiological investigation was carried out in a natural focus of tick-borne encephalitis infection in the region of the Krasnoyarsk hydroelectric construction site on the River Yenisei. The virus was isolated from 5 of 8 batches of ticks of the species *Ixodes persulcatus* comprising a total of 1,000 individuals collected on the right bank of the river, and from 1 of 12 batches totalling 544 individuals caught on the less populated left bank. In an investigation of 79 small mammals caught on the right bank the virus was isolated from the brain of an Altai pika (*Ochotona alpina hyperborea*). Neutralizing antibody to tick-borne encephalitis virus was found in the sera of 120 of 345 cattle (35%) from both banks of the river. *D. J. Bauer*

GREENWAY, D. J., RUGIERO, H. R., PARODI, A. S., FRIGERIO, M., RIVERO, E., DE LA BARRERA, J. M., GARZON, F., BOXACA, M., METTLER, N., DE GUERRERO, L. B. & NOTA, N. **Epidemic Hemorrhagic Fever in Argentina.** *Pub. Health Rep.* Wash. 1959, Nov., v. 74, No. 11, 1011–14. [14 refs.]

This disease apparently first appeared a few years before the present investigation of an epidemic in May 1958. There is a gradual onset of pyrexia, weakness, headache, myalgia, anorexia, vomiting, incoordination and sometimes strabismus. There may be a palatal enanthem but no rash. 3–5 days after onset the illness worsens with dehydration, rash, congestion and perhaps petechiae on the thorax and flanks. There may be epistaxis, haematemesis, melaena, haematuria and gingival haemorrhages: the Rumpel-Leede phenomenon [appearance of small haemorrhages under a rubber arm-band] is usually positive. There may be a cough but chest X-rays are normal. There is marked hypotension. The liver may be enlarged, there may be jaundice, oliguria and anuria may occur. Cutaneous hyperaesthesia, muscle spasms and spasms of the glottis occur and there may be stupor or delirium. Leucopenia may be marked and the platelet count may fall to 20,000 per ml. [? per cmm.]. The bone marrow shows hypofunction. The blood urea is increased and there is albuminuria with cellular and granular casts. Characteristically vacuolated epithelial cells are seen in the urine. At autopsy there is widespread vascular damage with interstitial oedema especially in the liver or kidneys. The brain is congested and there is marked meningeal oedema with mononuclear infiltration.

Virus has been isolated from blood, a suspension of viscera (brain, liver, spleen, kidney), and from urine containing a large amount of blood. Material was inoculated into mice, rats, guineapigs, hamsters, pigs, monkeys, chick embryos and tissue cultures of monkey kidney, HeLa and KB cells. Only guineapigs were affected: they sickened and died in 15—20 days and at necropsy had subcutaneous petechial haemorrages, haemorrhages in the abdominal lymph glands, and haemorrhages in the intestinal mucosa and in the adrenals. Neither bacteria nor fungi of aetiological importance were grown from either the patients or the guineapigs. A suspension of organs from an infected guineapig inoculated into suckling mice caused ataxia, spasms and occasionally paralysis on the 9th day. Later material from patients was also found to cause these effects in suckling mice. Suckling rats were also susceptible to brain from infected suckling mice. 56°C. for 30 minutes inactivates the virus which is also inactivated by ether and trypsin. Complement-fixation and neutralization tests demonstrated a rise in antibody in patients during the course of the disease. The disease was produced by inoculation of a human volunteer from whose blood the agent was isolated.

The disease predominantly affected rural labourers especially maize workers and occurred from April to July or August. In all age-groups males predominated, 45 of 73 patients being male. All the deaths were in males and the mortality rate was 23%. The virus is reported to have been isolated from *Mus. musculus, Hesperomys laucha* and *Akodon arenicola.* The virus is said to have been neutralized *in vivo* by Russian spring-summer antiserum [but the virus does not seem to beh like a member of the RSS group. Its desoxycholate sitivity does not appear to have been determined].

C. E. Gordon Smi

BECH, V. **Studies on the Development of Complem Fixing Antibodies in Measles Patients. Obse tions during a Measles Epidemic in Greenla** *J. Immunology.* 1959, Sept., v. 83, No. 3, 267- 6 figs. [17 refs.]

In autumn 1955 an epidemic of measles occurre Sukkertoppen, Greenland; there were 1,203 cases, only 4 presumed insusceptible persons escaped infect 212 samples of serum were taken from 71 patients 7 to 65 years at various stages of the illness and sen Denmark and the U.S.A. for examination. Complem fixing antibody appeared at the same time as or sh after the exanthem, and rose to a maximum titre of between the 5th and 16th days from the appearanc the exanthem. During the 22–34 days following development of the maximum titre a 2- to 8-fold decr in titre occurred in the majority of patients. No ris titre could be observed in 6 immune persons in wh families a case of measles had occurred. *D. J. Bau*

OBODOWSKA-ZYSK, Wanda. Powikłania ze str ośrodkowego układu nerwowego w odrze. **[C tral Nervous System Complications in Meas** *Przegląd Epidemiol.* Warsaw. 1959, v. 13, No 249–57. [45 refs.] English summary.

Among 170 patients with measles observed bet 1951 and 1957 8 developed signs of involvement of central nervous system. In 4 patients, aged 2½ years 19–21 years respectively, there was neck rigidity Kernig's sign, which appeared 1 day before the rash one patient and after 2–5 days in the remainder, las 1–4 days. 1 patient developed encephalopathy on 4th day of the exanthem, with recovery after 2 days. remaining 3 patients, aged 3½, 5 and 8 years, develo encephalitis 2–5 days after the appearance of the ex them; 1 patient died shortly after admission to hosp and the others recovered without sequelae after tr ment with cortisone. *D. J. Bau*

SIEGEL, M. & GREENBERG, M. **Fetal Death, Malfor tion and Prematurity after Maternal Rube Results of a Prospective Study, 1949–1958.** *N England J. of Med.* 1960, Feb. 25, v. 262, No 389–93. [13 refs.]

Of 5,457 cases of rubella in New York City in wo aged 15–44 years between 1949 and 1958 [see also *Bulletin,* 1958, v. 33, 96], 392 were identified as pregn at the time. Therapeutic abortion was performed in and in 20 the outcome of pregnancy was unknown. remaining 294 cases were followed up and observati made on the frequency of foetal deaths, major congen defects and prematurity. With rubella during the fir weeks of gestation half the pregnancies terminate

etal death compared with an expected 10—15% as imated by practising obstetricians [no control data re available]. Of 5 liveborn infants following rubella the first 4 weeks of gestation 3 were defective, of 20 th rubella in weeks 5—8 only 2 were defective, and of with rubella in weeks 9—13 none were defective. ubella took place in weeks 14—40 in 183 women but ly 2 of their infants were defective. The defects in e 5 early cases were those of eye or heart customarily corded after rubella but it is noticeable that all of em followed the 16 cases of rubella that occurred in 2 idemic years (1955 and 1958) and none the 9 cases of the inter-epidemic years. On the other hand this difference was not apparent with foetal death or with prematurity. In total, prematurity, as determined by a weight of 2,500 gm. or less, was observed in one-quarter of the 20 infants exposed to rubella in weeks 1—8. It appears to occur without detectable congenital malformations. *A. Bradford Hill*

SYMMERS, W. St. C. **Cytomegalic Inclusion-Body Disease affecting the Parotid Gland of an Adult.** *J. Path. & Bact.* 1960, Apr., v. 79, No. 2, 406–8, 3 figs. on pl.

Bacteriology and Immunity

The order in this section is:—**General; Bacteriostatic and Bactericidal Substances; Bacteria; Rickettsiae; Bacteriophages; Viruses; Immunity.**

Abstracts of papers relating to the bacteriology of plague, cholera, yaws, leprosy and certain other tropical bacterial diseases; of the rickettsial fevers; and of yellow fever, dengue, rabies and certain other tropical virus infections, are published in the TROPICAL DISEASES BULLETIN. *Their titles and page references are cited below in the appropriate sub-divisions of this section.*

GENERAL

TYLER, M. E.; SHIPE, E. L.; CHAPMAN, D. N.; PAINTER, R. B. **Bacterial Aerosol Samplers. I. Development and Evaluation of the All-Glass Impinger** [TYLER & SHIPE]. *Applied Microbiol.* Baltimore. 1959, Nov., v. 7, No. 6, 337–49, 13 figs. [34 refs.] **II. Development and Evaluation of the Shipe Sampler** [SHIPE, TYLER & CHAPMAN]. *Ibid.*, 349–54, 3 figs. **III. Comparison of Biological and Physical Effects in Liquid Impinger Samplers** [TYLER, SHIPE & PAINTER]. *Ibid.*, 355–62, 2 figs. [11 refs.]

I. The authors describe and illustrate a variety of uid-impinger type air samplers and report a number of mparative tests of their efficiency in collecting bacteria om artificially generated airborne clouds. A cotton-ool filter sampler was taken as the standard. The "all-ass impinger" was found to be highly efficient in llecting bacteria from the air, in that the proportion assing through it, and collected on the cotton-wool filter in in tandem, was only about 0·3%. The "midget npinger," in which the impingement velocity is lower an in the all-glass impinger, was less efficient in that out 10% of the cloud passed through it. However hen *Serratia marcescens,* in droplets greater than 3μ ean diameter, was used as the test organism the midget npinger gave a higher yield of viable organisms.

II. It was thought that the deficiencies of the all-glass npinger might be due to killing of the bacteria by im-ingement on the glass. The Shipe impinger was devised, onsisting of a conical flask with the air inlet arranged ear its base in such a way that the incoming air stream as tangential both to the wall and the floor of the flask and there was no inlet tube. This sampler only let pass between 1·7 and 4·2% of the test cloud and its recovery of *S. marcescens* particles was better than the all-glass impinger, especially for large-droplet clouds; it was about the same with *Bacillus subtilis* in small droplets.

III. A number of tests were also made to discover how much of the inefficiency of the all-glass impinger was due to loss in the inlet tube, using in particular dye-containing droplets as the test cloud. Below 5μ diameter practically all the droplets reached the collecting fluid, but with increase in size above this, there was increasing retention in the tubes. *S. marcescens,* in droplets trapped in the tube, died rapidly. By using radioactive tagged cells it was shown that there was also considerable death of *S. marcescens* cells at or after collection in the all-glass impinger, but less or none in the Shipe impinger.

In these 3 papers there is extensive discussion of the lack of general interest in fluid impinger samplers, compared with other instruments, for air sampling. This is attributed, partly, to wrong impressions of their efficiency as collecting devices. [They have, however, other serious disadvantages for field use in the study of naturally occurring infections because the volume of air sampled is too small to be useful for seeking pathogens; there is the need to prevent multiplication of the bacteria in the fluid after collection; and there is the need to process the sample on return to the laboratory. Impingers have, however, great advantages in experimental work where the bacterial count is expected to be high.

There is no mention of the paper by MAY and HARPER [this *Bulletin,* 1958, v. 33, 157] in which an extensive comparison of samplers is reported, and the defects of the all-glass impinger are demonstrated.]

R. E. O. Williams

WEBB, S. J. **Factors affecting the Viability of Air-Borne Bacteria. II. The Effect of Chemical Additives on the Behavior of Air-Borne Cells.** *Canadian J. Microbiol.* Ottawa. 1960, Feb., v. 6, No. 1, 71–87, 4 figs. [23 refs.] **III. The Role of Bonded Water and Protein Structure in the Death of Air-Borne Cells.** *Ibid.*, 89–105, 3 figs. [63 refs.]

II. Webb has previously suggested, from studies of the death rates of bacterial cells suspended in air at various relative humidities and temperatures, that death of air-borne cells is dependent on collapse of protein molecules following the loss of water [this *Bulletin*, 1960, v. 35, 594]. In these 2 detailed papers this thesis is further explored, first by measuring the death rate after the addition of various substances to the medium before spraying. Basic amino acids conferred some aerosol stability but less than peptone and similar polymers; native protein had no effect. Whereas in the presence of Bacto protone there was a steady decrease in the death rate with increasing humidity, the addition of sodium chloride not only increased the death rate at all humidities, but produced a peak in the region of 60%. Other chlorides had the same effect.

The addition of glycol and glycerol increased the death-rate after spraying, pentoses had no effect, but some hexoses decreased the death rate. Maximum protection was achieved with amino or secondary alcohol groups substituted on to a 6-membered ring nucleus, but the degree of protection varied with the humidity and with the period after spraying that was studied. Inositol was found to have a considerable protective effect which could be neutralized by urea or guanidine.

In discussion it is stressed that the effect of the medium from which bacteria are sprayed is very important in determining their survival and the products of metabolism could have a large effect. The protective action of some substance is postulated as due to their ability to replace water in the cell proteins and a particular structure may be needed so that the protein configuration is maintained.

III. The water content of air-dried bacteria was determined from dry weight and refractive index measurements. The death rate of air-stored cells was inversely correlated with their water content. Addition of NaCl to the suspending medium reduced the final water content considerably and was toxic to the cells; inositol had much less effect and was protective.

Strains of *Serratia marcescens* made resistant to chloramphenicol and other antibiotics were more resistant to aerosol death than sensitive strains, and a similar increase could be induced simply by suspension in the antibiotic before spraying. It is suggested that the drugs may act by combining with nucleoproteins. It is felt that the desiccation-sensitive structure in the bacterial cell may well be the protoplast membrane. *R. E. O. Williams*

SCHIRGER, A., MARTIN, W. J., ROYER, R. Q. NEEDHAM, G. M. **Bacterial Invasion of Bl after Oral Surgical Procedures.** *J. Lab. & C. Med.* 1960, Mar., v. 55, No. 3, 376–80. [13 re

This study was undertaken to compare the incide of bacteriaemia in patients who received no antibi before oral surgery with that in patients who recei phenoxymethyl penicillin orally for 24 hours be operation. None of the patients had cardiovasc lesions rendering them vulnerable to endocarditis. Gr A consisted of 50 patients who received no antibio Of these 27 had positive blood cultures immediately a operation. 10 cultures yielded *Streptococcus mitis* 1 yielded *Staphylococcus aureus.*

There were 50 patients in Group B and they recei 4 doses of 600 mgm. of phenoxymethyl penicillin (eq alent to 4,000,000 units) every 6 hours in the 24 ho before operation. 8 of these patients gave positive bl cultures immediately after operation but no streptoc were isolated.

The 27 patients in Group C received 4 doses of mgm. of phenoxymethyl penicillin (equivalent 2,000,000 units) every 6 hours in the 24 hours be operation. 5 of these patients gave positive bl cultures, 1 being due to *Strep. mitis.*

None of the patients whose blood cultures were p tive immediately after operation gave positive blood tures 18 hours after operation. The 3 groups were c parable with regard to the nature and extent of surgical procedures to which they were subjected.

The authors conclude that a total dose of 4,000 units of phenoxymethyl penicillin given orally in divi doses during the 24 hours before operation is as effec in decreasing bacterial invasion of the blood after surgery as other forms of penicillin given in diffe schedules. *R. J. Fallo*

SALTON, M. R. J. & PAVLIK, J. G. **Studies of the B terial Cell Wall. VI. Wall Composition Sensitivity to Lysozyme.** *Biochim. et Biop Acta.* 1960, Apr. 22, v. 39, No. 3, 398–407, 2 [31 refs.]

KÖHLER, W. Die pleuropneumonie-ähnlichen Mil organismen (PPLO). (Pleuropneumonia-like O nisms) Micromycetaceae. Sammelreferat. *Z. f. Bakt.* I. Abt. Ref. 1960, v. 175, No. 4, 305– [401 refs.]

LESSEL, E. F., Jr. **The Nomenclatural Status of Generic Names of the** *Actinomycetales.* *Inter Bull. Bact. Nomencl. & Taxon.* 1960, Apr. 15 10, No. 2, Suppl., 87–192. [Numerous refs.]

BACTERIOSTATIC AND BACTERICIDAL SUBSTANCES; DISINFECTION

The order in this section is:—**General; Antibiotics; Colicines; Other Therapeutic Substances; Disinfection.**

RIFFITH, R. S., with the technical assistance of Marjorie JOINER & Helen KOTTLOWSKI. **Comparison of Antibiotic Activity in Sera after the Administration of Three Different Penicillins.** *Antibiotic Med.* New York. 1960, Feb., v. 7, No. 2, 129–35.

This paper from the Lilly Laboratory for Clinical esearch, Indianapolis, reports the results of blood says ¼, ½, 1, 2, 4 and 6 hours after giving a single 250 gm. tablet of each of 3 forms of penicillin to 11 normal bjects. These forms were penicillin G, penicillin V nd alpha-phenoxyethyl penicillin ("Syncillin" in the .S.A., "Broxil" in Great Britain. The assays were done y a tube dilution method, with *Staphylococcus aureus* nd *Streptococcus pyogenes,* and results are given as ciprocals of the minimum inhibitory dilutions, *i.e.,* in rms of activity of the serum against these organisms nd not w/v concentrations. The levels achieved with exceeded those with G because of better absorption. omparison of V levels with those attained by alpha-henoxyethyl penicillin showed that of V to be consider-bly higher initially, but about the same at 1, 2 and 4 ours. Alpha-phenoxyethyl penicillin has been claimed produce higher blood levels than V. It is pointed out ere that this apparent advantage is neutralized by its rrespondingly lesser antibacterial activity. "We must nphasize that before a new form of an antibiotic is sumed to be better than another, the antibacterial tivity of both in the sera must be compared against presentative pathogenic bacteria." *L. P. Garrod*

ITRI, N. **Cellbound Penicillinase and Exopenicillinase in the γ-State.** *Bull. Res. Counc. of Israel.* 1960, Apr., v. 9A, Nos. 1/2, 28–34, 3 figs. [10 refs.]

ROHASKA, E. & BRUNNER, R. Über die resistenzvermindernde Wirkung oberflächenaktiver Stoffe, insbesonders von Netzmitteln bei penicillinresistenten Staphylokokken. [**On the Action of Surface-active Substances, particularly wetting Agents, in diminishing the Resistance of Penicillin-resistant Staphylococci**] *Zent. f. Bakt.* I. Abt. Orig. 1959, v. 176, Nos. 7/8, 455–67. [18 refs.]

According to these authors, who write respectively om Vienna and Kundl, Tyrol, sodium lauryl sulphate as been shown by earlier workers to inactivate "coli-enicillinase" ("clarase"). They decided to ascertain hether this applies also to staphylococcal penicillinase, nd examined a series of anionic and non-ionic surface-ctive agents for capacity to inactivate penicillinase xtracted from staphylococci. Many of them possessed is property: furthermore, when added to culture edium, many of them greatly reduced the concentration f penicillin required to inhibit the growth of a resistant strain. Since they were not inhibitory in themselves, and only slightly increased the sensitivity of some sensitive strains, it is concluded that they render staphylococci more vulnerable to penicillin by inactivating penicillinase as it is formed by a living culture. [The original paper should be consulted for information about the identity of the numerous substances tested. Some are given descriptive chemical names, others only proprietary ones, which with the exception of Lissapol and Tween are unfamiliar]. *L. P. Garrod*

NAUMANN, P. & MAI, K. Wirkstoffspiegel und mikrobiologische Grundlagen der intramuskulären Chloramphenicol-Therapie. [**Serum Concentrations and Microbiological Basis of Intramuscular Chloramphenicol Therapy**] *Deut. med. Woch.* 1959, Nov. 6, v. 84, No. 45, 2013–18, 2059–60, 6 figs. [18 refs.]

These authors from Hamburg begin by praising chloramphenicol as an antibiotic with a broad spectrum (embracing staphylococci as well as enterobacteria) to which bacterial resistance is uncommon. Oral administration is not always feasible, and they therefore studied the action of "Paraxin intramuskular," a preparation for injection [the solvent in this is not specified]. The antibiotic was assayed in the blood by the *Bacillus subtilis* cup plate method and chemically. After a single dose of 1 gm., the blood level at 2 hours was about 10 μgm./ml., falling to 3 μgm./ml. at about 8 hours. Findings after repeated doses are also given: there appears to have been no cumulative effect. The minimum inhibitory concentrations of chloramphenicol for multiple strains of 6 species of bacteria were determined and these are represented in an ingenious diagram (Fig. 6) on which a curve of blood concentrations is superimposed. It is concluded that for infection by an organism inhibited by 4 μgm./ml., a dose of 1 gm. at 12-hour intervals should be adequate, but less sensitive organisms may demand that this interval be shortened to 6 hours. *L. P. Garrod*

SAZ, A. K. & MARTINEZ, L. Marina. **Enzymatic Basis of Resistance to Aureomycin. III. Inhibition by Aureomycin of Protein-Stimulated Electron Transport in** *Escherichia coli. J. Bacteriology.* 1960, Apr., v. 79, No. 4, 527–31, 2 figs. [12 refs.]

ARCAMONE, F., BERTAZZOLI. C., GHIONE, M. & SCOTTI, T. Amminosidina. Un nuovo antibiotico oligosaccaridico. [**Amminosidine, a New Oligosaccharide Antibiotic**] *Giorn. di Microbiol.* Naples. 1959, Oct.–Dec., v. 7, No. 4, 251–72, 6 figs. [21 refs.] English summary.

PURKAYASTHA, M. & NANDI, P. **Survey of Antibiotic-Producing Bacteria from the Soils of India and Indonesia.** *Antibiotics & Chemotherapy.* New York. 1960, Apr., v. 10, No. 4, 242–8, 2 figs. [18 refs.]

FRIEDMAN, Dvora R. & HALBERT, S. P. **Mixed Bacterial Infections in relation to Antibiotic Activities. IV.** *Shigella-Escherichia coli* **Infections.** *J. Immunology.* 1960, Jan., v. 84, No. 1, 11–19, 4 figs. [53 refs.]

This is a continuation of previous work by Halbert on the interference of one bacterial species with the growth of another within the body, whether in the bowel or elsewhere (some of his previous papers are concerned with such possibilities in the conjunctival sac, and he writes from the Department of Ophthalmology Research in Columbia University, New York). The present experiments were of 2 kinds. Adult mice were inoculated intraperitoneally with both *Shigella paradysenteriae* III [?*S. flexneri 3*] and *Escherichia coli*, the latter being either an antibiotic (colicine)-producing strain or not. Mice were killed at intervals of 2, 4, 6 and 8 hours and cultures were made from peritoneal washings in which the 2 organisms were enumerated. When the *E. coli* was not a colicine producer both multiplied; when it was, the *E. coli* multiplied and the *Shigella* diminished in numbers, and colicine was demonstrable even after 2 hours in the exudate.

In the second series of experiments, mice 2–3 days old were infected orally with a virulent *E. coli* with or without admixture of larger numbers of another strain, either colicine-producing or not, the virulent organism being susceptible to the colicine. Results were judged by mortality. They were somewhat different in 2 strains of mice, but they gave no clear evidence of inhibition of the virulent strain by colicine, since the mortality was a little lower when the second strain was added whether it was a colicine-producer or not. The colicine-producer was shown by cultivating rectal swabs to have established itself in the bowel. *L. P. Garrod*

THON, D. & NEUMANN, M. Erfahrungen mit der Sterilisierung durch Aethylenoxyd. [**Experiences with Sterilization by Ethylene Oxide**] *Zent. f. Bakt.* II. Abt. 1959, v. 113, Nos. 1/5, 114–27 figs. [35 refs.]

The authors are on the staff of the Membrane Fi Company, Göttingen, and their main interest is in sterilization of the products of this firm. They us chamber of 1 cubic metre capacity in which a vacuur drawn and ethylene oxide gas then admitted: after 6 hc it is pumped out and replaced by sterile air. degree of humidity is said to be indifferent within w limits, and ambient temperature was found satisfact Membrane filters contaminated with various vegeta or sporogenous bacteria were regularly sterilized b concentration of 1200 gm. ethylene oxide per cubic mc Culture media could also be sterilized, and became a able of supporting normal growth 1 or 2 days la Further experiments with cartons used for dried m showed that the method is also suitable for objects c posed of cellulose. *L. P. Garro*

LAMMERS, T., DAY, H., KÖRNLEIN, M. & SEIBEL, Neuartige Äthylenoxyd-Desinfektion bei Staph kokkenhospitalismus. [**A New Method of Ethyl Oxide Disinfection in Connexion with Staph coccal Hospital Infection**] *Ztschr. f. Hyg. Infektionskr.* 1960, v. 146, No. 3, 236–43, 1 [13 refs.]

The ingenious proceeding described here is inter for pillows, blankets, etc., from the beds of infe patients, with particular reference to staphyloco infection. They are simply placed in a gas-tight pl bag, which is then blown up from a cylinder with ethylene oxide in CO_2 and left for 48 hours. It sh then still be distended: if collapsed it has leaked. F ments of fabric contaminated with staphylococcus ture placed anywhere within the contents (even in interior of feather pillows) were regularly sterilized wi this time when the ambient temperature was 21°C. 10°C. they were not, because ethylene oxide conde at this temperature. Some Gram-negative species killed under the same conditions in 24 hours. It was shown that the gas would disinfect pieces of cork w had been soaked in staphylococcus culture. The me is unsuitable for anything made of rubber, since absorbs the gas. *L. P. Garro*

BACTERIA

The order in this section is:—**Cocci; Donovania; Mycobacterium; Corynebacterium; Haemophilus; Pseudomonas; Pfeifferella; Enteric Organisms; Brucella; Pasteurella; Bacillus; Anaerobes; Spirochaetes; Erysipelothrix; Listeria; Others.**

HOEPRICH, P. D., CROFT, G. F. & WEST, L. M. **Tellurite Reduction as an Indicator of Potentially Pathogenic Staphylococci.** *J. Lab. & Clin. Med.* 1960, Jan., v. 55, No. 1, 120–28, 3 figs. [24 refs.]

259 strains of staphylococci from clinical specin and 73 from cultures of the antecubital skin of no people, were tested for coagulase production, abilit grow on the tellurite-glycine medium of ZEBOVITZ e

is *Bulletin,* 1956, v. 31, 671], mannitol fermentation, emolysis, pigmentation and gelatinase activity. Strains om pus were the most active. Of 251 strains from nical specimens, 191 were coagulase positive and 193 ew on the tellurite medium and reduced the tellurite; 8 did both. Tellurite reduction might therefore be ed as an alternative to coagulase production for distinishing the potentially pathogenic strains. The telrite-glycine medium was found to be too inhibitory to used for primary isolation. *R. E. O. Williams*

RK, J. T. & HANCOCK, R. **A Fractionation Procedure for Studies of the Synthesis of Cell-Wall Mucopeptide and of Other Polymers in Cells of** *Staphylococcus aureus.* *J. General Microbiol.* 1960, Feb., v. 22, No. 1, 249–58, 2 text figs. & 1 pl. [31 refs.]

GELSANG, T. M. & ÖSTERVOLD, B. **The Stability of Staphylococcal Phage Typing.** *Acta Path. et Microb. Scandinavica.* 1959, v. 47, No. 4. 364–72.

The authors discuss the variation in results of repeated age typing of single strains of staphylococci and give amples of results of typing single colonies. They stress e importance of frequent control of the routine test lution [RTD] on each batch of medium and suggest at if there is any doubt if 2 strains are the same they ould be retested on the same day with the same phage eparation and media.

Only very minor differences in the strength of some actions were obtained on typing a streptomycin-sensire strain of Group III and its resistant variant produced the laboratory and between a streptomycin-sensitive ain of a Group I/III strain and its resistant variant. The occurrence of strains of types 80 and 52/52A/80 s noted in the nose and throat of patients and staff one hospital and in strains from lesions in another spital. The type 80 strains were not lysed by phages or 52A even at RTD x 1000 and it was concluded at these strains were different [ASHESHOV and RIPPON is *Bulletin,* 1959, v. 34, 1175), also noted the occurnce of strains of type 52/52A/80 in outbreaks of type infection and showed that, in the laboratory, strains type 80 can be converted to type 52/52A/80 by sogenization]. *M. Patricia Jevons*

CHMIDT, J. Über die Differenzierung des *Staphylococcus aureus* und den Wert der Lysotypie bei der Aufklärung epidemiologischer Zusammenhänge von Staphylokokkeninfektionen, insbesondere Mastitiserkrankungen. [**The Differentiation of** *Staphylococcus aureus* **and the Value of Phage typing in the Elucidation of the Epidemiolcgical Relations of Staphylococcal Infections, especially Mastitis**] *Arch. f. Hyg. u. Bakt.* 1960, Feb., v. 144, No. 1, 17–31. [31 refs.]

After a long discussion of various methods for distinishing strains of *Staph. aureus,* especially phage typing, the author reports the typing and antibiotic-sensitivity testing of 189 strains isolated in a maternity hospital epidemic; 83 of the strains were from breast abscesses. 56 of the mastitis staphylococci were phage type 52/80+ and 13 had the very similar pattern 52/52A/79/80; 65 of these 69 strains were penicillin-resistant. Of 37 strains from skin, mucous membranes and dust, 16 fell into the epidemic type. *R. E. O. Williams*

LACHOWICZ, T. & ROMANOWSKI, T. Charakterystyka bakteriofagowa nosicielstwa gronkowcowego u dzieci. [**Bacteriophage Characteristics of the Staphylococcal Carrier-State in Children**] *Med. Dośw. i Mikrob.* Warsaw. 1959, v. 11, No. 3, 213–20. [35 refs.] English summary (8 lines).

The authors have subjected 737 strains of staphylococci isolated from the nasopharynx of child carriers to typing with 30 staphylococcal type phages. In a preliminary examination with the routine test dilution of phage 460 strains (62·4%) could be typed; 207 of the strains which did not react could be typed with undiluted phage, and 45 others reacted with an additional range of phages, giving a total of 712 strains (96·6%) which could be typed. *D. J. Bauer*

LACHOWICZ, T. Badania serologiczne nad nosicielstwem gronkowcowym. [**Serological Investigations on the Carrier State of Staphylococci**] *Med. Dośw. i Mikrob.* Warsaw. 1959, v. 11, No. 3, 221–6. [23 refs.] English summary (9 lines).

652 strains of staphylococci isolated from child carriers were subjected to typing in slide agglutination tests with standard immune sera. 229 (35·12%) were of type 2, 48 (7·36%) of type 1 and 35 (5·06%) of type 3. 271 strains were resistant to penicillin, including 72 of type 2, and 28 were resistant to streptomycin. *D. J. Bauer*

LACHOWICZ, T. Badanie bakteriofagowe i serologiczne gronkowców izolowanych od nosicieli. [**Bacteriophage and Serological Investigations of Staphylococci isolated from Carriers**] *Med. Dośw. i Mikrob.* Warsaw. 1959, v. 11, No. 3, 227–31. English summary (9 lines).

In a continuation of the work described in the preceding paper a comparison has been made of the results obtained by the serological and phage-typing methods in the classification of 659 strains of staphylococci isolated from carriers. According to the results of phage-typing 459 strains belonged to group I and 99 to group III, whereas according to agglutination tests serotype 2 was most frequent, with 231 strains, followed by type 1 with 47 strains and type 3 with 32. Agreement between the two methods of classification was only observed in 9·26% of instances. Only 0·45% of strains were untypable by the phage method compared with 13·65% by the serological method. *D. J. Bauer*

LACHOWICZ, T. Z badań nad antagonistycznymi szczepami gronkowcowymi. [**Studies on Antagonistic Strains of Staphylococci**] *Med. Dośw. i Mikrob.* Warsaw. 1959, v. 11, No. 3, 233–6. [10 refs.] English summary.

Among 1,223 strains of staphylococci isolated from patients and carriers in 1947 and 1955–57 84 showed antagonistic properties. The proportion of antagonistic strains fell gradually during the period concerned, from 20 (11·92%) [*sic*] of 218 strains in 1947 to 50 (7·1%) of 742 in 1955 and 12 (4·56%) of 263 in 1956–57. All the 1947 strains were sensitive to penicillin, whereas 5 of the 1955 and 9 of the 1956–57 strains showed varying degrees of resistance. 58 (70·73%) strains were of phage-type I, and 10 (12·19%) were of phage-type II, and according to serological investigations 47 (60·25%) were of serotype 2.

D. J. Bauer

PRIGAL, S. J. **Bacteriophage Typing of Staphylococci from Asthmatic Patients. Seventh of a Series on Bacteriological and Epidemiologic Approach to Treatment of Sinorespiratory Infections.** *J. Amer. Med. Ass.* 1960, Mar. 26, v. 172, No. 13, 1361–7, 3 figs.

Staphylococci from people subject to sino-respiratory infections and from their families were bacteriophage-typed. Strains from 115 people, 95 of whom were members of 27 families were examined and the families fell into 2 groups; colonized families where 2 or more members carried staphylococci of the same type, and non-colonized families.

85·7% of the 42 people in the 12 colonized families carried staphylococci and there were 11 asthmatic patients in this group 9 of whom had symptoms. Only 58·5% of the 41 members of 12 non-colonized families carried staphylococci, 5 of them had asthma but 4 were asymptomatic at the time of swabbing. No one type of staphylococcus was found to be related to infectious asthma. Four detailed case histories are given.

M. Patricia Jevons

KARSKA, Barbara, KOZAK, W., NARBUTOWICZ, Barbara & STOLARSKA, Anna. Lizogenia gronkowców. [**Lysogenicity of Staphylococci**] *Med. Dośw. i Mikrob.* Warsaw. 1960, v. 12, No. 2, 137–46. [19 refs.]

The English summary appended to the paper is as follows:—

"The examination of lysogenicity of staphylococci was employed for: (1) determination of pathogenicity of strains, (2) supplementation of classification by means of phage-typing, (3) analysis of the results of phage-typing.

"Lysogenicity of 187 coagulase-negative and coagulase-positive strains of staphylococci was examined.

"In 100% of coagulase-negative strains (out of 65 examined) the lack of ability to liberate virus particles was observed.

"'Lysogenicity pattern' of 76% coagulase-posit strains was determined (out of 122 examined strains).

"By means of phage-typing 19% of coagulase-nega and 80% coagulase-positive strains were classified. E ploying both, the coagulase test and phage-typing, 9 strains were classified as potentially pathogenic.

"Moreover it was found that by introducing the t 'lysogenicity pattern' it is possible to divided the sa lytic types into smaller subgroups.

"The appearance of prophage immunity was obser in 62% of coagulase-positive lysogenic staphyloco Susceptibility to homologous phage was found in 40% coagulase-positive strains.

"The causes of these phenomena are discussed."

D'ANTONA, D., PIAZZI, S. E. & SALETTI, M. S titolazione della tossina stafilococcica alfa, con metodo emolitico. [**On the Titration of the Al *Staphylococcus* Toxin by the Haemolytic Meth** *Ann. Sclavo.* Siena. 1959, Nov.–Dec., v. 1, No 583–616, 9 diagrams. [28 refs.] English summ

The methods of determining haemolytic activity the neutralizing capacity of antistaphylococcal sera the haemolysin are carefully studied. The chief con sions reached are that the suspension of the rabbit bl used should be carefully standardized by haematocrit by colorimetric determination of haemoglobin con after saponin haemolysis: a 1% suspension and ¾-hou water-bath at 37°C., followed by 14 hours overnigh the refrigerator at 4°C. are recommended. After period of cooling the titre is always higher than removal from the incubator.

A number of graphs are produced in which the amo of toxin required to produce all degrees of haemol from 0 to 100% in the presence of antitoxin are re sented. These show that the concentration at which antitoxin is used in the range 1 unit to 1/25 unit ha considerable effect on the amount of toxin neutrali the apparent neutralization and hence potency of serum being greater at the lower level of antitoxin c centration.

Although a standard of 50% heamolysis as determi with the colorimeter is accepted as the ideal level reading such observations on neutralization, it is clai that the rougher method of visual observation gives sults which diverge only slightly provided the read are taken at the level of no haemolysis rather than of 100% haemolysis.

A further point brought out in these observations neutralization of haemolysin is that the diverg between readings made immediately after incubation those made after cooling overnight is much greate low than at high concentrations of antiserum. The a serum appears to be considerably more potent whe reading is made after ¾-hour at 37°C. The general c clusion is drawn that a rigid correspondence in all de of technique is essential before the observations on t tions of different sera can be correlated.

J. W. McLe

ohn, H. P. & Kienitz, M. Über den Nachweis des Staphylokokken-Enterotoxins. 4. Untersuchungen an Staphylokokken-Stämmen von eitrigen Erkrankungen und gesunden Keimträgern. [**On the Demonstration of Staphylococcal Enterotoxin. 4th Communication: Investigation with *Staphylococcus* Strains isolated from Pus and from Healthy Carriers**] *Zent. f. Bakt.* I. Abt. Orig. 1960, v. 177, No. 4, 555–9. [11 refs.]

Kienitz and Preuner [this *Bulletin*, 1959, v. 34, 574, 9] tested 101 strains of staphylococcus in the embryoted hen's egg, in the belief that a lethal effect on the abryo denoted enterotoxin production. The present per reports the phage typing of the 12 strains found ositive in this test. 8 fell into phage-group III, while the other strain were distributed over the phage groups in e usual way. Feeding tests for enterotoxin production ere not carried out. *R. E. O. Williams*

orse, S. I. **Isolation of a Phagocytosis-Inhibiting Substance from Culture Filtrates of an Encapsulated *Staphylococcus aureus*.** [Correspondence.] *Nature*. 1960, Apr. 2, v. 186, 102–3, 1 fig.

Alcohol precipitation was used to extract a fraction om the culture supernatant of an "encapsulated" rain of *Staphylococcus aureus*. The deproteinized aterial gave a precipitate with homologous rabbit antira and absorbed from the sera their power of agglutiting a suspension of the Smith strain, and their psonizing power [Cohn and Morse, this *Bulletin*, 1960, 35, 389]. *R. E. O. Williams*

eld, Julia T. & Rogers, D. E. **Staphylococcal Immunity: Production of Staphylococcal Hemagglutinins in Rabbits receiving Staphylococcal Vaccine.** *Proc. Soc. Exper. Biol. & Med.* 1960, Feb., v. 103, No. 2, 311–14, 3 figs.

Vaccines of heat-killed 4-hour and 18-hour broth cultres of *Staphylococcus aureus* strain Giorgio (phage pe 47/53/54/75) were prepared and used to immunize bbits. Injections were at intervals of 7–10 days by travenous, subcutaneous, intradermal or intraperitoneal utes; total amounts of vaccine given were the same in ch set of rabbits. Animals were bled before and during mmunization and sera were tested by the heamagglutiation test.

Red cell sensitizing antigens were prepared from the iorgio strain in 4 different ways. Haemagglutinins were etectable in sera of rabbits receiving both types of accine at 14—22 days and were maximal in 30 to 40 days itre 1/2560): response was swifter and higher in rabbits eceiving intravenous injections. A red cell concentration f 1·25% cells and undiluted sensitizing antigen from pernatant of heat-killed 18-hour cultures gave optimal sults in the test. Supernatants from living 4-hour cultres were unsatisfactory sensitizing antigens owing to e haemolysis of the red cells by exotoxin. Sera agglutated cells sensitized with antigens prepared from 5 heterologous coagulase-positive strains and 1 coagulase-negative strain but to a lower titre.

M. Patricia Jevons

Weaver, J. K. & Middlebrook, G. **Experimental Penicillin Prophylaxis of Staphylococcal Infection in Rabbits.** *Proc. Soc. Exper. Biol. & Med.* 1960, Jan., v. 103, No. 1, 108–11.

Suture material was soaked in a broth culture of a penicillinase-producing strain of staphylococcus of phage type 80 which had been grown for 2 hours with (P) and without penicillin (NP).

This material was used to close surgical wounds in the backs of rabbits. The infecting dose of organisms was calculated by taking the difference between counts on identical lengths of suture material soaked in broth and counts on remnants of material used to close wounds, which had been similarly treated. The infecting dose was always less than 1000 viable units.

Wounds were sutured with NP and P cultures alternately, each animal having 4 wounds. 1 group of rabbits were treated with penicillin 4 days before and 2 days after infection.

All wounds in untreated animals (11 P and 11 NP) became infected and the time of onset and clinical course was the same in both groups. 2 of 10 wounds infected with NP cultures in animals receiving penicillin became infected as did 10 of 11 wounds infected with P cultures. Wounds infected with P cultures were clinically more severe. There was no evidence of genetic change in bacterial populations recovered from the animals.

These results suggested that staphylococci previously exposed to penicillin have a greater capacity to start infection than those which have not been exposed even if penicillin treatment is given. Provided inoculum is small and penicillin dosage adequate, penicillin treatment is effective in preventing wound infection due to a resistant strain not previously exposed to penicillin.

M. Patricia Jevons

Daikos, G. K., Athanasiadou, Maria & Foutzopoulou, E. Empfindlichkeit pathogener Staphylokokken gegenüber Ristocetin und anderen chemotherapeutischen Mitteln. [**Sensitivity of Pathogenic Staphylococci to Ristocetin and other Chemotherapeutic Agents**] *Ztschr. f. Hyg. u. Infektionskr.* 1959, v. 146, No. 2, 161–5, 1 fig. [10 refs.]

These observations were made with 100 strains of coagulase-positive staphylococci isolated during the summer and autumn of 1958 from in-patients in a hospital in Athens. Sensitivities were determined by cultivation on solid media containing concentrations falling by 2-fold from 20 μgm./ml. Only 17% were inhibited by even the highest concentrations of penicillin, which, as the authors remark, shows an exceptionally high frequency of penicillin resistance. The order of activity of the antibiotics tested was novobiocin>erythromycin>tetracycline and oleandomycin>chloramphenicol and ristocetin. The curves of frequency distribution of different degrees of

resistance to the 2 latter were almost identical, 95 and 97% of strains being inhibited by 10 μgm./ml., and 41% in each case by 5 μgm./ml. Tests were also done with sulphamethoxypyridazine, in concentrations falling from 10 mgm./ml., and no inhibition of any strain was observed [the significance of this depends on the composition of the culture medium, and particularly on the size of the inoculum, neither of which is specified].

L. P. Garrod

Kowalska, Janina & Pakuła, R. Badania nad receptorem bakteriofagowym u *Streptococcus pyogenes*. [**Studies on the Bacteriophage Receptor in** *Streptococcus pyogenes*] *Med. Dośw. i Mikrob.* Warsaw. 1959, v. 11, No. 3, 255–66, 1 fig. [28 refs.] English summary.

The authors have investigated the relation between the polysaccharide and protein fractions of types A and C streptococcus and the type-specific A25 and C4 phages. The polysaccharide was obtained by extraction of the bacterial cells with 0·2 N HCl at 100°C., followed by neutralization and precipitation with acetone, or by enzymatic lysis or treatment with formamide. C4 phage was almost completely inactivated by incubation with C polysaccharide from the C4 strain of streptococcus for 15–60 minutes at 37°C., whereas A polysaccharide from the A25 strain of streptococcus had no effect upon A25 phage. In adsorption experiments with 6 strains of type A and 4 strains of type C streptococci it was found that all strains would adsorb A25 phage irreversibly irrespective of whether they were sensitive to it or not. The ability to adsorb phage was not affected by removal of M and T proteins by treating the bacteria with trypsin, or by removal of nucleoproteins by extraction with 0·01 N NaOH for 10 minutes at 100°C. Treatment with 0·2 N HCl at 100°C. caused a progressive loss of the ability to adsorb phage; it was possible to isolate a protein from the acid extract which inactivated both phages, and a protein with a similar effect upon the streptococcal phages could also be obtained from staphylococci.

D. J. Bauer

Otto, Rosemarie. Experimentelle Untersuchungen über die Streptokokkengruppenpräzipitation im Agargel. [**Experiments on Agar Gel Precipitation of Streptococcal Group Antigens**] *Zent. f. Bakt.* I. Abt. Orig. 1960, v. 177, No. 4, 546–54, 5 figs. [12 refs.]

Acid and formamide extracts of streptococci of various groups formed good precipitin lines with group-specific antisera in various agar gels in Petri dishes. It is suggested that this might be used for routine identification of the strains [despite the fact that the test takes 24–48 hours instead of 15 minutes]. No satisfactory precipitin lines were obtained when group sera were tested against growing cultures or washings of grown cultures.

R. E. O. Williams

Bernheimer, A. W. & Schwartz, Lois L. **Leucoci Agents of Haemolytic Streptococci.** *J. Path. Bact.* 1960, Jan., v. 79, No. 1, 37–46. [18 refs.

Streptococcal extracellular products were studied their effect on polymorphonuclear leucocytes. A drop mouse blood was put on a coverslip and after clot retr tion red cells were removed by washing. Coverslips w adherent leucocytes were mounted on slides, sealed, kept at 37°C. for use.

Streptolysin O was found to be leucocidal and to p duce definite changes within 60 minutes. Various p parations of streptolysin O were titrated for leucoci activity by counting the number of damaged and nor cells. The leucocidal activity for which cysteine necessary ran parallel to the haemolytic activity and to the diphosphopyridine nucleotidase (DPNase) activ This activity could be neutralized by serum contain antistreptolysin O. Streptolysin S was also leucocidal the cytological changes differed from those produced streptolysin O.

Erythrogenic toxin, streptococcal proteinase, strepto nase, hyaluronidase, DPNase and streptococcal deoxyri nucleases had little or no effect on leucocytes. Cr concentrated preparations of various types of Group streptococci showed no additional leucotoxic ag except a type 12 strain which is being further investiga

M. Patricia Jevon

Lacks, S. & Hotchkiss, R. D. **A Study of the Gen Material determining an Enzyme Activity** *Pneumococcus. Biochim. et Biophys. Acta.* 19 Apr. 22, v. 39, No. 3, 508–18, 8 figs. [15 refs.]

Lund, Erna. **Diagnosis of Pneumococci by the Op chin and Bile Tests.** *Acta Path. et Mic Scandinavica.* 1959, v. 47, No. 3, 308–15.

All of 50 S strains of pneumococci and all of 1 strains were inhibited by Optochin at a concentration 2·5 μgm./ml. in blood agar or 5·0 μgm./ml. in se broth, and in diffusion tests with tablets contai 0·05 mgm., or paper discs moistened in 0·05% Optoc None of 80 strains of [presumably α-haemolytic] stre cocci were inhibited at these concentrations. 77 str of streptococci belonging to defined groups or spe were also tested; only 17% gave any significant de of inhibition with the disc test. All the S pneumoc were bile soluble but some R strains were not, thc still Optochin sensitive and typable by capsule swel

R. E. O. Willian

Jyssum, K. **Assimilation of Nitrogen in Menin cocci grown with the Ammonium Ion as Nitrogen Source.** *Acta Path. et Microb. Sca navica.* 1959, v. 46, No. 4, 320–32, 4 figs. refs.]

Previous work [this *Bulletin*, 1943, v. 18, 339; 194 21, 145] has shown that with fluid media glumatic ac essential for the growth of meningococci. 3 strains

en continuously grown (daily subculture) for 3 months a minimal salt medium containing thiosulphate, $CaCl_2$, and glucose, solidified with 1·5% agar and with NH_4Cl as the sole source of N. As a prerequisite to owth on this medium, the strains were adapted to metalize glucose (maltose could be substituted) by growing blood agar glucose plates. This adaptation was essenl to get colony formation with a critical minimum of 000—1,500 cells plated per petri-dish. Non-adapted ains, *i.e.*, freshly isolated and not utilizing glucose, will ow and give colonies only with very much larger ocula. The NH_4Cl could be replaced by $(NH_4)_2SO_4$ d when the strains were used to this the thiosulphate uld be omitted from the medium, but the resulting owth was poorer and the colonies smaller.

In a study of the N uptake by the meningococci, cell-e extracts of both the adapted and non-adapted strains ere shown to contain a TPN catalysed glumatic dehydronase; there was no significant difference between the oups in the activity of the enzyme system. Furtherore with these cell-free extracts transaminase reactions ok place between α-oxoglutaric acid and aspartic acid, anine and several other amino acids, producing glumatic id and the corresponding keto acids.

The paper should be read for technical details.

Elizabeth M. Harper

ATLIN, B. W. **Transformation of *Neisseria meningitidis* by Deoxyribonucleates from Cells and from Culture Slime.** *J. Bacteriology.* 1960, Apr., v. 79, No. 4, 579–90, 1 fig. [20 refs.]

"Highly polymerized deoxyribonucleate (DNA) is a mponent of the slime which may accumulate in cultures *Neisseria meningitidis* as cellular viability declines. To ivestigate possible genetic activity of such extracellular NA, a quantitative transformation method was deve-ped. Various factors were studied which influence ansformation of streptomycin-sensitive meningococci to reptomycin resistance: cellular competence, time of xposure and concentration of transforming DNA, and henotypic expression. Transformation of a streptoycin-dependent meningococcus strain to nondependence, lso, was studied.

"Extracellular DNA was separated by ethanol precipitation from the supernatant broth of centrifuged slimy ultures (streptomycin-resistant strain cultivated in brain eart infusion broth at 37°C. for 2 to 4 days). Intracellur DNA was extracted from detergent-lysed cells. Solutions of partially purified DNA preparations obtained rom the two locations exhibited similar transforming ctivities. Moreover, crude culture slime, in dilutions as igh as 1:25, elicited about the same number of transormants as were obtained using transforming DNA preparations, tested at a concentration of 5 μg. DNA per ml. Thus, procedures for extracting and purifying the DNA ere not required for demonstrating transforming activity f extracellular DNA. The possibility was discussed that atural variation of meningococci, and perhaps of other acteria, may be enhanced through the agency of transormation by slime layer DNA."

HIRSCH, H. A. & FINLAND, M., with the technical assistance of Clare WILCOX. **Susceptibility of Gonococci to Antibiotics and Sulfadiazine. A Study of Strains isolated at Boston City Hospital from Cases of Acute Gonorrheal Urethritis in Males, August, 1958 to February, 1959.** *Amer. J. Med. Sci.* 1960, Jan., v. 239, No. 1, 41–50, 5 figs. [21 refs.]

Strains of gonococci isolated between August 1958 and February 1959 from cases of acute gonorrhoea in the male in Boston were tested for sensitivity to 20 antibiotics and to sulphadiazine. Results with penicillin are given for 157 strains, with other important antibiotics and sulphadiazine for 132, and with antibiotics of lesser importance for smaller numbers. The most interesting findings are those with penicillin and sulphadiazine, and these are compared with results obtained in the same laboratory in 1949 and 1954. There is a trend towards diminished sensitivity to penicillin, some strains requiring 0·1 and even 0·2 μgm./ml. to inhibit their growth: the higher the inhibitory concentration the more often were the strains derived from patients in whom treatment failed. An opposite change was seen with sulphadiazine: whereas in 1949 most strains were highly resistant, the majority are now sensitive, and rather more so than in 1954. There was no significant change in the general level of susceptibility to any other antibiotic. There are some interesting details with regard to the relative activity of antibiotics forming groups: thus erythromycin is much more active than spiramycin, oleandomycin or carbomycin, demethylchlortetracycline is slightly more active than the other 3 tetracyclines, and kanamycin than neomycin or paromomycin.

L. P. Garrod

BERENESI, G., HIDEG, K. & VECSEY, Z. Über die technische Verwendung des Cetyl-pyridiniumbromid zur Homogenisierung in der bakteriologischen Diagnose der Tuberkulose. **[Technical Application of Cetyl-Pyridinum-Bromide for Homogenization in Bacteriological Diagnosis of Tuberculosis]** *Zent. f. Bakt.* I. Abt. Orig. 1960, v. 178, No. 3, 332–6. [17 refs.]

The English summary appended to the paper is as follows:—

"The authors homogenised the sputa for cultivation of the mycobacterium tuberculosis with 1% watery cetylpyridinum bromide solution (sterogenol). This method has the following advantages: (1) The method primarily saves time, (2) neutralization after homogenization is superfluous, possible sources of error thus being eliminated, (3) the mycobacterium tuberculosis practically remains intact if this method is used in spite of 24 hours of homogenisation, (4) contamination of media is eliminated to a great extent, (5) the percentage of Koch-positivity practically remains undisturbed."

NORMAN, J. O. & WILLIAMS, R. P. **The Use of Egg-Yolk Dialysate for the Growth of** *Mycobacterium tuberculosis*. *Amer. Rev. Respiratory Dis.* 1960, Mar., v. 81, No. 3, 423–5, 1 fig.

The dialysate was obtained from the sterile egg yolk which had been exhaustibly extracted with ether and dialysed in Cellophane bags suspended in sterile water for 1 week at 37°C. The residue was discarded and 10% of the sterile dialysate was added to Proskauer and Beck medium.

Measured by the increase in optical density, H37Rv and a non-photochromogenic mycobacterium showed a marked increase in growth after 12 days' incubation in the supplemented medium as compared with the poor growth that occurred in plain medium. This enhanced growth did not occur when the dialysate was diluted 1:100 for H37Rv, or 1:1000 for the non-photochromogen, and although the enhancement was not lost for the latter organism when the dialysate was autoclaved or exposed to acid or alkali, it was abolished for H37Rv by either of these treatments. The enhancement also occurred when the dialysate was added to the solid medium consisting of 2% agar in Proskauer and Beck medium, the growth then being superior to that on Löwenstein-Jensen or ATS egg medium.

The stimulating factor present in the dialysate is apparently not cholesterol or oleic acid, and its relationship to the stimulating polysaccharide from tender coconuts is being investigated. *S. R. M. Bushby*

KUPER, S. W. A. & MAY, J. R. **Detection of Acid-Fast Organisms in Tissue Sections by Fluorescence Microscopy.** *J. Path. & Bact.* 1960, Jan., v. 79, No. 1, 59–68, 8 figs. [6 (5 coloured) on 2 pls.]

This method uses dark-ground microscopy and the bacilli are stained with auramine to which rhodamine has been added to impart a reddish tinge to the yellow fluorescent image. The illumination is from a high-pressure mercury vapour lamp, filtered through a copper sulphate solution, and as ultraviolet light plays little part in exciting fluorescence of this dye, the absorption of light of this wave-length by the optical system is irrelevant. A cardioid dark-ground condenser and a 2 mm. oil immersion objective, suitably stopped, or for most routine purposes a 3·6 mm. oil-immersion objective (N.A. 0·90) is used, and in order to reduce the blue light coming from non-fluorescent objects a yellow filter is inserted in the eyepiece.

Numerous preparations containing *Mycobacterium tuberculosis*, *Myco. leprae* and *Myco. johnei* were examined in the course of developing the technique. Fixation with formalin and Zenker fluid gave equally brilliant fluorescence, but staining at 37°C. or 56°C. was a little superior to staining at room temperature. Investigation into the use of the usual acid-alcohol and potassium permanganate differentiation showed that the role of permanganate was to lessen fluorescence from the background, and therefore decolorization with other agents is apparently unnecessary. Dehydration can either be with alcohol or by blotting, but prolonged treatment with alcohol tends to reverse the effect of the permangana 15 seconds is adequate. "Fluorment" mountant is commended but after 1–2 weeks it was found to deve some greenish fluorescence. Either glycerol or liq paraffin is suitable as the immersion fluid, but so batches may fluoresce. [A recommended procedure sections is described in detail, and the method is rec mended for the examination of sputum, cultures tissue smears in leprosy.] *S. R. M. Bushb*

DISSMANN, E. & ZECHNER, E. Zur Frage der Diff enzierung humaner und boviner Tuberkelbakter mit Hilfe von Thiophen-2-carbonsäurehydra (TCH) nach Boenicke. [**Boenicke's Thiopher Carbonic Acid Hydrazide Test for Differen tion of Human and Bovine Tubercle Baci** *Ztschr. f. Hyg. u. Infektionskr.* 1960, v. 146, No 210–14, 1 diagram.

Most tests for differentiation of bovine from hun tubercle bacilli have broken down latterly on accoun the effect on strains of treatment with isoniazid.

Of 555 primary cultures submitted to Boenicke's (failure to grow in Löwenstein-Jensen media contain 10 μgm. of thiophen-2-carbonic acid hydrazide per cc. were determined to be bovine but on repeated subcult on media free from this substance, only 2 persisted sensitive and presumably bovine. *J. W. McLeo*

KONNO, K., NAGAYAMA, H. & OKA, S. **Differentiat of Bovine Tubercle Bacilli from other My bacteria by the Determination of Nicotinamid Activity.** *Amer. Rev. Respiratory Dis.* 1960, A v. 81, No. 4, 550–54, 2 figs.

"The nicotinamidase activity of cell-free extracts f various mycobacteria was determined qualitatively quantitatively.

"Only bovine tubercle bacilli, irrespective of virule and isoniazid susceptibility, reveal significantly lo nicotinamidase activity than other mycobacteria. nicotinamidase activity of human, avian, and unclassi mycobacteria is more than 30 times that of bovine bac while that of non-pathogenic acid-fast bacilli is 60 ti greater. Thus, bovine tubercle bacilli, both virulent attenuated, irrespective of isoniazid resistance, can distinguished from other mycobacteria by determi the nicotinamidase activity of cell-free extracts of bacteria."

GUTIÉRREZ-VÁZQUEZ, J. M. **Further Studies on Spot Test for the Differentiation of Tube Bacilli of Human Origin from other My bacteria.** *Amer. Rev. Respiratory Dis.* 1 Mar., v. 81, No. 3, 412–14.

The purpose of this paper was to provide additio evidence for the accuracy and reliability of this test *Rev. Lat.-Amer. Microbiol.*, 1958, v. 1, 287).

The test consists of adding 0·5–0·8 ml. of distilled water to a well grown culture on Löwenstein-Jensen medium, autoclaving at 15 lb. for 15 minutes, and placing on a porcelain spot-test 2–4 drops of the extract and 0·05 ml. of a 1·5% alcoholic solution of *o*-tolidine plus a similar volume of 10% aqueous solution of cyanogen bromide. By this method the extracts from 52 human strains of tubercle bacilli and H37Rv and R1Rv gave a red coral colour within 4 minutes, whereas those from 10 strains of bovine bacilli, 3 strains of avian bacilli, 10 strains of unclassified mycobacteria and 3 strains of saprophytic mycobacteria gave either no colour, a light blue or only a light dirty pink colour. Further tests showed that variations in *p*H between the values of 3 and 9 had no effect on the reaction and positive results were obtained with cultures stored for up to 250–300 days.

The author claims that this test for niacin production is simple, rapid and easily reproducible.

S. R. M. Bushby

Williams, C. A., Jr. **Studies on Fractions of Methanol Extracts of Tubercle Bacilli. II. Toxic and Allergenic Properties of Fractions employed as Antituberculous Vaccine.** *J. Exper. Med.* 1960, Mar. 1, v. 111, No. 3, 369–86, 2 figs. [15 refs.]

In a previous paper [this *Bulletin*, 1960, v. 35, 501] the author, and a collaborator, reported that a partially purified methanol extract of tubercle bacilli was capable of inducing an increase in the resistance of mice to experimental tuberculosis. The extract was shown to contain 2 fractions which when used together produced a higher degree of protection than when used separately, fraction F I acting as the antigen and fraction F II as the adjuvant.

The primary extract is obtained by continuous methanolic extraction of killed, vacuum-dried, acetone "defatted" bacilli, and it is fractionated into 3 parts by low concentration at 45–50°C. The first fraction, F I, was slightly soluble in petroleum ether and the third fraction, F IV, was the highly concentrated residue. F I, can be subfractionated by adding ethanol to 33% and NaCl to 0·5% concentrations; F I-P was the insoluble fraction and F I-S the soluble fraction.

These fractions have now been tested for various properties, and although each was not submitted to the same tests, the results show that:—

(1) Injected intracutaneously into guineapigs, F I causes some local damage: (F II and F IV may be similarly toxic but they were only tested at lower doses).

(2) Injected intraperitoneally into mice F IV causes a marked loss of weight whereas F I-P causes only a moderate loss; there is some evidence to indicate that the toxic effect of F I-P depends upon previous exposure of the animals to mycobacteria.

(3) Injected simultaneously with living staphylococci, intravenously, both F I and F II depress the resistance of mice to the infection, but the depression by subfraction, F I-S, is much less than that by F I-P.

(4) Judged by the ability of the fractions to interfere with the effect of fresh serum to inactivate the TR2+ coliphage, the activity of properdin is readily neutralized by F I-P and insignificantly by F I-S.

(5) F IV and, to a lesser extent, F I are capable of inducing an allergic skin reaction in tuberculin-sensitive guineapigs.

(6) F I-P, but not F I-S, acts as a Freund-like adjuvant when injected with killed BCG, the BCG being essential for inducing the sensitization.

(7) When injected with picrylated homologous red cell stroma, F I and F II are incapable of acting as the whole mycobacteria of Freund's adjuvant.

From the result of previous experiments the author had considered F II to act as an adjuvant for F I in inducing immunity, but the failure of F II to act as an adjuvant for picryl chloride, indicated that the adjuvant action is not of general applicability. In the author's opinion the results of the present experiments show that F I-S possessed only slight, if any, toxic or allergenic properties and that it therefore qualifies as a suitable non-living vaccine against tuberculosis.

S. R. M. Bushby

Schaefer, W. B. **Effect of Isoniazid on the Dehydrogenase Activity of** *Mycobacterium tuberculosis.* 1960, Feb., v. 79, No. 2, 236–45, 7 figs. [38 refs.]

"Tubercle bacilli exposed to bactericidal concentrations of isoniazid or α-ethyl-thioisonicotinamide in an environment favorable for growth showed an early stimulation of their dehydrogenase activity followed by a decrease and loss of this property. It is suggested that these drugs inhibit the synthesis of a lipid component in the membranes of tubercle bacilli and that the process of unbalanced growth resulting from this inhibition is the cause of irreversible injury to the bacterial cells. Evidence in favor of this hypothesis is discussed."

Willett, Hilda P. **The Production of Lysine from Diaminopimelic Acid by Cell-Free Extracts of** *Mycobacterium tuberculosis. Amer. Rev. Respiratory Dis.* 1960, May, v. 81, No. 5, 653–9, 2 figs. [12 refs.]

Tárnok, I. Serologische Aktivität der Mycobacterium-Desoxyribonuklein-Säuren. **[Serological Activity of Deoxyribonucleic Acid of Mycobacteria]** *Zent. f. Bakt.* I. Abt. Orig. 1960, v. 178, No. 4, 576–7. [10 refs.]

Beck, A. **Skin Sensitisation of Guinea-Pigs with Atypical Acid-Fast Bacilli.** *J. Path. & Bact.* 1960, Apr., v. 79, No. 2, 285–8.

"Quantitative skin sensitivity tests, with protein fractions of 4 strains of atypical acid-fast bacilli and of other mycobacteria, in guineapigs infected with these bacilli revealed marked cross-reactivity of these antigens. A quantitative evaluation of these tests suggests that atypical acid-fast bacilli form a serological group which can be distinguished from both tubercle bacilli and saprophytic mycobacteria."

AGARWAL, S. C. **Effects of Diphtheria Toxin on Acetylcholine Synthesis.** *J. Path. & Bact.* 1960, Apr., v. 79, No. 2, 313–18.

"Diphtheria toxin reduces the in-vitro synthesis of acetylcholine by rat-brain slices and acetone-dried guinea-pig brain powders. It does not affect the conversion of bound into free acetylcholine, nor does it inhibit the formation of acetylcholine from choline chloride and acetate in reaction mixtures. It is suggested that diphtheritic paralysis may be due to diminished synthesis of acetylcholine in nerve cells, due to a deficiency in the parent substrates responsible for acetylcholine synthesis. The deficiency of the substrate may be due to a block in the metabolic activity of the cell."

DE BOCK, C. A. & WORST-VAN DAM, A. M. **Fixation of the Agglutinogen from** *Hemophilus pertussis* **on the Bacterial Surface.** *Antonie van Leeuwenhoek: J. Microbiol. & Serol.* 1960, v. 26, No. 1, 126–8.

"The agglutinogen of *Hemophilus pertussis* is rather soluble in some suspending media but can be fixed on the bacterial surface with formaldehyde in saline."

HIRSCH, H. A. & FINLAND, M., with the technical assistance of Clare WILCOX. **Susceptibility of** *Hemophilus influenzae* **to 21 Antibiotics** *in vitro*. *Amer. J. Med. Sci.* 1960, Jan., v. 239, No. 1, 33–40, 1 fig.

Strains of *Haemophilus influenzae* isolated in January and February 1959 from clinic material (chiefly bronchial secretion, but including a few from blood or cerebrospinal fluid) were tested for sensitivity to 21 antibiotics. The results are compared with those of similar surveys conducted in this laboratory in 1949 and 1954, and no tendency towards increase in resistance to any antibiotic is revealed. The antibiotics with the lowest inhibitory concentrations were penicillin, novobiocin and polymyxin, in that order of activity. Within groups of antibiotics, erythromycin was much more active than spiramycin, oleandomyin or carbomycin, and demethylchlortetracycline slightly more active than the other 3 tetracyclines. Colimycin was less active than polymyxin. The neomycin group and several less known antibiotics were included in the tests. *L. P. Garrod*

CHAMBON, L. Analyse sérologique de l'antigène somatique de *Malleomyces pseudomallei*. [**Serolcgical Analysis of the Somatic Antigen of** *Malleomyces pseudomallei*] *Ann. Inst. Pasteur.* 1960, Mar., v. 98, No. 3, 405–15.

[An abstract of this paper appeared in the *Tropical Diseases Bulletin*, 1960, v. 57, 851.]

LEVINE, H. B. & WOLOCHOW, H. **Occurrence of Poly-β-Hydroxybutyrate in** *Pseudomonas pseudomallei*. *J. Bacteriology*. 1960, Feb., v. 79, No. 2, 305–6.

LEGLER, F., BURKHARDT, F. & EHRMANN, A. Beitr zur Frage der optimalen Nährbodenkombination der *Salmonella-Diagnostik*. [**The Optimal Comb nation of Culture Media for the Isolation Salmonellae**] *Zent. f. Bakt.* I. Abt. Orig. 19 v. 177, No. 4, 559–64. [19 refs.]

The authors have analysed the results of several yea routine work to assess first, whether Endo agar still h a place in the diagnosis of salmonella infection, and s ondly the relative value of the Wilson and Blair mediu the Leifson deoxycholate citrate agar and the Preuss tet thionate medium. In 1955-6 a series of 30,069 specime were cultured on all 4 media. By using Endo agar, t authors isolated 2 out of a total of 116 paratyphoid strains, 6 out of 168 *Salm. typhi-murium* and 2 out of *Salm. enteritidis* strains that would otherwise have be missed. The use of Endo agar might thus be justifi *e.g.* in the investigation of large food-poisoning outbrea

The culture findings on a series of 73,637 specime nearly all stools or urines, are also tabulated. The f lowing table gives the numbers of strains of the mo important pathogens isolated, together with the perc tages of successful isolations from the different media.

Organism	Total No.	Percentage positive Tetrathionate	W & B	wit Leifs
Salm. typhi	543	45·4	63·5	80·6
Salm. paratyphi B	346	79·2	46·5	60·4
Salm. typhi-murium ...	396	80·6	47·7	34·9
Salm. enteritidis	145	76·6	43·4	48·3
Other salmonellae	571	77·7	47·1	47·9

The percentages of positive results obtained on c medium only of the 3 used in this series were as follo for the pathogens listed as before:

Organism	Tetrathionate	W & B	Leifsc
Salm. typhi	7·9	8·1	19·2
Salm. paratyphi B	25·7	4·6	8·4
Salm. typhi-murium... ...	37·6	11·9	4·3
Salm. enteritidis	34·5	8·3	8·9
Other salmonellae	31·2	7·0	9·2

The authors comment on the excellent results obtain with deoxycholate citrate agar in the isolation of typh bacilli. Paratyphoid bacilli were also isolated more re ily on this medium than were the food-poisoning salm ellae. For all salmonellae except the typhoid bacill tetrathionate medium gave very similar percentages positive results. *B. Moor*

BUONOMINI, G., GABBRIELLI, G. & SALETTI, M. Pri osservazioni su di un vaccino antitifico allestito c terreno semi-sintetico. [**Preliminary Observatio on a Typhoid Vaccine prepared on a Part defined Medium**] *Ann. Sclavo.* Siena. 19 Nov.–Dec., v. 1, No. 6, 637–46. [20 refs.] Engl summary.

The medium suggested has the following formula:—

Bacto casamino acids (Difco) ...	5 gm.
Sodium lactate (50%)	12 cc.
Magnesium *sulphate*	0·1 gm.
Potassium chloride	0·1 gm.
Nicotinic acid	0·005 gm.
Water	1000 cc.

Autoclave at 121°C. for 20 minutes and then add 0·5% of a solution sterilized by Seitz filtration containing:—

Tryptophane	1·2 gm.
Calcium pantothenate	0·12 gm.
Water	100 cc.

It will grow the typhoid strain used in adequate amount if strongly aerated and can be shown to be free from pyrogenic effects by observations on the reactions of men inoculated (the extreme reaction recorded was 38·8°C.).

Definite evidence of the development of protective antibodies in the subjects inoculated was obtained by the increased doses of typhoid bacilli tolerated by chick embryos which had passive protection from the sera of the inoculated. The survival of mice protected by the sera of rabbits inoculated with this vaccine was limited however—2% in 50 controls and 7% in 100 "protected" mice. Observations on the active immunization of mice with this vaccine was more promising however.

Extended investigation of such vaccine is indicated.

J. W. McLeod

BUONOMINI, G., GABBRIELLI, G. & SALETTI, M. Sui metodi di preparazione e di controllo dei vaccini antitifici. [**Methods of Preparation and of Control of Efficiency of Antityphoid Inoculation**] *Ann. Sclavo.* Siena. 1959, Nov.–Dec., v. 1, No. 6, 617–36. [30 refs.] English summary.

The chief points made are that the strain used should be capable of stimulating antibody formation to both O and Vi antigens. The strain Ty 2 is suitable. Sterilization by various methods gives results which are very similar provided there is no undue damage to the antigens. Agents which can be satisfactorily used are alcohol, acetone and formaldehyde.

The production of agglutinins in injected rabbits is not a reliable guide: but the protective qualities of the sera of immunized rabbits, if tested on white mice by the technique of FELIX [this *Bulletin*, 1952, v. 27, 85] or on chick embryos by the technique of GRABAR and LE MINOR [*Ibid.*, 367] furnish valuable indications of the quality of the antigen used to immunize the rabbits.

Results obtained by these tests correspond closely to those obtained in the active immunization of mice which are subsequently injected with a test dose of living bacilli. Mucin should not be used in such tests.

Of all these methods of control, that of the passive protection of chick embryos is the most satisfactory on account of the ease with which large numbers of examinations can be carried out with small amounts of serum. In this respect it is specially useful in estimating the success of human antityphoid inoculations.

Fluid vaccines deteriorate rapidly at room temperature, but remain potent for at least 12 months if kept at +4°C. The ultimate solution of the problems of preservation is now being sought in the use of lyophilized products.

J. W. McLeod

ZINDER, N. D. **Sexuality and Mating in** *Salmonella*. *Science.* 1960, Mar. 25, v. 131, 924–6. [17 refs.]

"Another criterion for the presence of the agent (F) promoting genetic exchange in *Escherichia coli* was found. It involves a staining reaction of Hfr and F+ coli, but not F– coli, when mixed with strains of *Salmonella typhimurium*. This reaction was used as a guide in following the transfer of the F agent to *Salmonella* and back to *E. coli*. The F agent in *Salmonella* seems to promote the same kinds of events that it promotes in *E. coli*."

LINDE, K. Ein experimenteller Beitrag über die Virulenzabhängigkeit der Para-B Bakterien (*S. paratyphi B*) von der Wachstumsphase. [**An Experimental Observation on the Relationship of Virulence and Growth Phase of Typhoid B bacilli** (*Salm. paratyphi B.*)] *Ztschr. f. Hyg. u. Infektionskr.* 1960, v. 146, No. 3, 195–201. [26 refs.]

Inoculation of amounts of culture which contain equal numbers of living *Salm. paratyphi B* has shown that bacteria taken in the log phase of growth are more virulent than those taken in the phase of decrease of living bacteria.

This is analogous to findings with regard to Gram-positive bacteria such as the pneumococcus.

J. W. McLeod

LINDE, K. Der Einfluss der Vermehrung von *Streptomyces albus* in einer absterbenden Para-B-Kultur (*S. paratyphi B*) auf das Virulenzverhalten der Salmonellen. [**The Effect on the Virulence of the Salmonella of growing Streptomyces Albus in Dying Culture of** *Salmonella paratyphi B*] *Ztschr. f. Hyg. u. Infektionskr.* 1960, v. 146, No. 3, 202–9, 3 figs. [37 refs.]

If a suspension of *Salm. paratyphi B* (in Koser solution) which is dying off is inoculated with *Streptomyces albus* the virulence of this material for guineapigs is increased and if used to inoculate nutrient broths it shows a decreased time of latency in developing growth compared with an aliquot part of the suspension in Koser solution which has not had *Streptomyces albus* added. A suggested explanation is that some of nutrient liberated in process of digestion of dead salmonellae by *Streptomyces albus* is available for growth of surviving salmonellae.

J. W. McLeod

STEHR, K. Beiträge zur Biologie der *Salmonella paratyphi B.* III. Mitteilung. Agglutinations-, Präzipitations- und Komplementbindungsversuche mit Lithium- und Caesiumformen der *Salmonella paratyphi B.* [**Contributions to the Biology of** *Salmonella paratyphi B.* **IIIrd Communication: Agglutination-, Precipitation- and Complement-Fixation Tests with Lithium and Caesium Forms of** *Salmonella paratyphi B*] *Zent. f. Bakt.* I. Abt. Orig. 1960, v. 177, No. 4, 564–75.

MIYAKE, T. **Mutator Factor in** *Salmonella typhimurium*. *Genetics.* 1960, Jan., v. 45, No. 1, 11–14.

WATANABE, T. **Transductional Studies of Thiamine and Nicotinic Acid requiring Streptomycin Resistant Mutants of** *Salmonella typhimurium*. *J. General Microbiol.* 1960, Feb., v. 22, No. 1, 102–12, 1 fig. [16 refs.]

BERRY, L. J. & BEUZEVILLE, C. **The Effect of Delayed Injections of Tricarboxylic Acid Cycle Inhibitors and Reticuloendothelial "Blocking" Agents on** *Salmonella typhimurium* **Infection in Mice.** *J. Infect. Dis.* 1960, Mar.-Apr., v. 106, No. 2, 183–92, 6 figs. [23 refs.]

SMITH-KEARY, P. F. **A Suppressor of Leucineless in** *Salmonella typhimurium*. *Heredity*. 1960, Feb., v. 14, Pts. 1/2, 61–71. [15 refs.]

USHIBA, D., SAITO, K., AKIYAMA, T., NAKANO, M., SUGIYAMA, T. & SHIRONO, S. **Studies on Experimental Typhoid: Bacterial Multiplication and Host Cell Response after Infection with** *Salmonella enteritidis* **in Mice immunized with Live and Killed Vaccines.** *Japanese J. Microbiol.* 1959, Apr., v. 3, No. 2, 231–42, 4 figs.

Comparable batches of mice were immunized with a heat-killed vaccine prepared from a smooth highly virulent strain of *Salmonella enteritidis* and a living vaccine prepared from a non-motile R type mutant of low virulence obtained from the previous strain. Both batches of test mice and a suitable number of comparable controls were challenged with the highly virulent strain. The essential difference in the results of the two immunization procedures was that bacterial multiplication in the spleen was markedly inhibited after the first day in mice inoculated with the living vaccine whereas, in mice immunized with the heat-killed vaccine, the challenge organisms in the local body fluid, *e.g.*, peritoneal fluid, were killed off within 12 hours. The killed vaccine failed to inhibit the multiplication of the bacteria in the spleen and there was no reduction of the organisms in the peritoneal fluid following at an early stage after intraperitoneal challenge of mice immunized with the living vaccine.

Since the protective effectiveness of the living vaccine was markedly superior to that of the killed vaccine it is concluded that inhibition of bacterial multiplication in the parenchymal organs rather than in the body fluids is essential for the protection of the mouse against infection with *Salm. enteritidis*. *H. J. Bensted*

ANZ, W. & MAJER, M. Über die Isolierung einer schleimigen Variante der Salmonella Manchester. [**Isolation of a Mucous Variant of Salmonella Manchester**] *Zent. f. Bakt.* I. Abt. Orig. 1960, v. 178, No. 3, 321–4, 1 fig.

"Report is given on the isolation of an O-inagglutinable, mucous variant of S. manchester from a purulent pleural fluid obtained by puncture and from an empyema of the gall bladder. In both cases the S. manchester strains cultivated from the stool in question grew in th normal form."

GUELIN, A. & LÉPINE, P. Fixation comparée du radi phosphore par des bactéries vivantes et des bactéri tuées. [**Comparative Fixation of ^{32}P by Livi Bacteria and by Killed Bacteria**] *Ann. In Pasteur.* 1960, Feb., v. 98, No. 2, 242–51, 1 f [11 refs.]

The amount of phosphorus fixed by bacteria varies accordance with whether they are alive or dead. For t most part the fixation of phosphorus is more intense living than by dead bacteria and more intense in org nisms in the logarithmic phase than those in the stationa phase. The particular organism studied by the autho was *Shigella dysenteriae* strain Y6R and the results their experiments suggest that the assimilation of mine phosphorus is not so wide as is generally thought a that only a part of the ^{32}P is fixed on the bacteria. *H. J. Benstea*

SERÉNY, B. Keratoconjunctivitis shigellosa. [**Kera conjunctivitis Shigellosa**] *Zent. f. Bakt.* I. A Orig. 1960, v. 178, No. 3, 325–31. [32 refs.]

The English summary appended to the paper is follows:—

"Shigella strains, freshly isoalted from feces, produ a keratoconjunctivitis shigellosa in guinea pigs. So salmonella types may induce only conjunctivitis witho keratitis. Keratoconjunctivitis shigellosa may be used the determination of freshly isolated Shigella strains.

"In guinea pigs infected for the first time keratoc junctivitis shigellosa is a disease taking a course of ch acteristic consecutive phases. It is followed by immun based on humoral and tissue factors. After the heal of a keratoconjunctivitis shigellosa successful reinfectio show a great variability of the clinical picture.

"Antibiotic treatment proved to be ineffective. A v low natural resistance seems to be the cause of this the peutic failure. Vaccines proved to have no prophyla effect on keratoconjunctivitis shigellosa."

MACKEL, D. C., WEAVER, R. E., LANGLEY, Lorreine & DE CAPITO, Thelma M. **Observations on Occ rence in Cats of** *Escherichia coli* **Pathogenic Man.** *Amer. J. Hyg.* 1960, Mar., v. 71, No. 176–8.

"Examination of 103 cats from veterinary hospit and pounds in the vicinity of Phoenix, Ariz., yielded isolations (15 types) of recognized or suspected types *Escherichia coli* pathogenic for man."

WEIDEL, W., FRANK, H. & MARTIN, H. H. **The Ri Layer of the Cell Wall of** *Escherichia* **Strain B.** *J. General Microbiol.* 1960, Feb., v. No. 1, 158–66, 7 figs. on 2 pls. [14 refs.]

ANDERSON, P. A. & PETTIJOHN, D. E. **Synchronization of Division in** *Escherichia coli. Science.* 1960, Apr. 15, v. 131, 1098, 1 fig.

"The smallest cells of a culture in the logarithmic phase, when isolated by a single rapid filtration through 2-μ Millipore paper, show good synchronization and reproducibility through the first division cycle. The method minimizes metabolic shock and provides a culture in which an easily reproducible initial state is established at a known time."

WEINBERG, R. **Gene Transfer and Elimination in Bacterial Crosses with Strain K-12 of** *Escherichia coli. J. Bacteriology.* 1960, Apr., v. 79, No. 4, 558–63. [23 refs.]

ALPER, T. & GILLIES, N. E. **The Relationship between Growth and Survival after Irradiation of** *Escherichia coli* **Strain B and Two Resistant Mutants.** *J. General Microbiol.* 1960, Feb., v. 22, No. 1, 113–28, 13 figs. [28 refs.]

HERRMANN, R. Immunologisches Verhalten von Nucleinsäuren aus E coli. I. Mitteilung: Versuche über die Antigenität. [**Immunological Behaviour of Nucleic Acids from** *Escherichia coli.* **I. Studies on Antigenicity**] *Zent. f. Bakt.* I. Abt. Orig. 1960, v. 179, No. 1, 86–92. [16 refs.]

STRAUSS, B. & OKUBO, S. **Protein Synthesis and the Induction of Mutations in** *Escherichia coli* **by Alkylating Agents.** *J. Bacteriology.* 1960, Apr., v. 79, No. 4, 464–73, 5 figs. [14 refs.]

VIJESUNDERA, S. & WOODS, D. D. **Suppression of Methionine Synthesis in** *Escherichia coli* **by Growth in the Presence of this Amino Acid.** *J. General Microbiol.* 1960, Feb., v. 22, No. 1, 229–41, 2 figs. [18 refs.]

MOROWITZ, H. J. & SPAULDING, Marie. **A Statistical Analysis of the Order of Certain Amino Acids in the Protein of** *Escherichia coli. Biochim et Biophys. Acta.* 1958, Sept., v. 29, No. 3, 514–21, 4 figs. [15 refs.]

FORRO, F., Jr. & WERTHEIMER, S. A. **The Organization and Replication of Deoxyribonucleic Acid in Thymine-Deficient Strains of** *Escherichia coli. Biochim. et Biophys. Acta.* 1960, May 6, v. 40, No. 1, 9–21, 11 figs. [20 refs.]

MANDELSTAM, J. & HALVORSON, H. **Turnover of Protein and Nucleic Acid in Soluble and Ribosome Fractions of Non-Growing** *Escherichia coli. Biochim. et Biophys. Acta.* 1960, May 6, v. 40, No. 1, 43–9. [18 refs.]

KEPES, A. Études cinétiques sur la galactoside-perméase d'*Escherichia coli.* [**Kinetic Studies on the Galactoside-Permease in** *E. coli*] *Biochim. et Biophys. Acta.* 1960, May 6, v. 40, No. 1, 70–84, 11 figs.

SISTROM, W. R. **On the Physical State of the Intracellularly Accumulated Substrates of β-Galactoside-Permease in** *Escherichia coli. Biochim. et Biophys. Acta.* 1958, Sept., v. 29, No. 3, 579–87, 4 figs.

WIESMEYER, H. & COHN, M. **The Characterization of the Pathway of Maltose Utilization by** *Escherichia coli.* **I. Purification and Physical Chemical Properties of the Enzyme Amylomaltase.** *Biochim. et Biophys. Acta.* 1960, Apr. 22, v. 39, No. 3, 417–26, 7 figs. [15 refs.] **II. General Properties and Mechanism of Action of Amylomaltase.** *Ibid.*, 427–39, 9 figs. [16 refs.] **III. A Description of the Concentrating Mechanism.** *Ibid.*, 440–47, 6 figs.

MUSCHEL, L. H. **Bactericidal Activity of Normal Serum against Bacterial Cultures. II. Activity against** *Escherichia coli* **Strains.** *Proc. Soc. Exper. Biol. & Med.* 1960, Mar., v. 103, No. 3, 632–6. [11 refs.]

"Resistance to bactericidal action of normal human serum of *L. coli* isolates from normal children and from those with diarrhoea was determined. Results indicated that serum resistance did not provide a basis of differentiation of virulent and non-virulent strains. Serum resistance was associated with the O-inagglutinability of the organisms. In addition, bactericidal action of normal human serum against *E. coli* was shown to be dependent upon natural antibodies of marked specificity."

HORMAECHE, E. & EDWARDS, P. R. **A Proposed Genus** *Enterobacter. Internat. Bull. Bact. Nomencl. & Taxon.* 1960, Apr. 15, v. 10, No. 2, 71–4.

The name *Aerobacter aerogenes* has given rise to much trouble in bacteriology. Used for non-motile, Gram-negative rods that do not liquefy gelatin it is a later synonym of *Klebsiella pneumoniae.* Recently HORMAECHE and EDWARDS [this *Bulletin,* 1958, v. 33, 979] proposed that the name should be used for motile rods with IMViC reactions − − + +. To reduce confusion these authors now withdraw their 1958 proposal, and suggest that the motile forms (both gelatin-liquefying and non-liquefying) should be placed in a new genus *Enterobacter* [not *Enterobacter* Rahn] with *Enterobacter cloacae* (Jordan) nov. comb. as type species, the non-liquefying form to be known as *E. aerogenes* (Hormaeche and Edwards 1958) nov. comb. Type cultures are available from the

National Collection of Type Cultures in England and the American Type Culture Collection in U.S.A.

[The proposal raises a difficulty not mentioned by the authors. It is usual for the name of a family to be derived from the name of a genus in the family, thus Pseudomonadaceae from *Pseudomonas*. Enterobacteriaceae is an exception and is not derived from *Enterobacter*; as an exception it was the subject of Official Opinion No. 15 in which the genus *Escherichia* was designated as type genus.] *S. T. Cowan*

HORMAECHE, E. & EDWARDS, P. R. **Proposal for the Rejection of the Generic Name *Cloaca* Castellani and Chalmers, and Proposal of *Enterobacter* as a Generic Name with Designation of Type Species and of its Type Culture. With Request for an Opinion.** *Internat. Bull. Bact. Nomencl. & Taxon.* 1960, Apr. 15, v. 10, No. 2, 75–6.

Because confusion has arisen over the name *Aerobacter aerogenes* a request has been made to the Judicial Commission of the International Committee on Bacteriological Nomenclature for an Official Opinion.

Aerobacter Beijerinck is a later synonym of *Klebsiella* Trevisan, and *Aerobacter* Hormaeche and Edwards was restricted to motile organisms, and was intended to embrace the gelatin-liquefying and non-liquefying strains of the genus *Cloaca*. It is pointed out that *Cloaca cloacae* is almost a tautonym (a name where the generic and specific names are the same) and thus should be rejected under Rule 25 of the Bacteriological Code.

The authors of the request want to test the reaction of bacteriologists to their proposal that *Enterobacter* be used for certain motile organisms (see the previous paper). *S. T. Cowan*

KRCMÉRY, V. Vplyv izonikotínhydrazidu a p-amínosalicylovej kyseliny na metabolické reakcie a katalázovú a peroxydázovú aktivitu brucel. [**Influence of Izonicotinhydrazide and p-Aminosalicylic Acid on Metabolic Reactions and on Catalase and Peroxidase Activity of Brucellae**] *Československ. Epidemiol., Mikrobiol., Imunol.* Prague. 1960, v. 9, No. 3, 173–7. [36 refs.] English summary (9 lines).

TALBOT, J. M. & SNEATH, P. H. A. **A Taxonomic Study of *Pasteurella septica*, especially of Strains isolated from Human Sources.** *J. General Microbiol.* 1960, Feb., v. 22, No. 1, 303–11, 1 fig. [28 refs.]

"The characteristics of 59 strains of *Pasteurella septica*, mostly derived from human lesions, were analysed by an electronic computer. The cat strains showed a high degree of similarity to each other, while the dog strains were more variable. Most human infections other than those due to bites seem to be due to strains which probably originated from cats. The analysis suggests that *P. septica* is distantly related to *P. pestis* and *P. pseudotuberculosis* but that the two latter are closely related to each other."

BURROWS, T. W. & BACON, G. A. **V and W Antige in Strains of *Pasteurella pseudotuberculosis*.** *Br J. Exper. Path.* 1960, Feb., v. 41, No. 1, 38–4 1 fig. [15 refs.]

Previous studies by these authors [see *Trop. Dis. Bu* 1954, v. 51, 793, 794; 1956, v. 53, 1424; 1957, v. 54, 28 showed that if virulent and avirulent strains of *Paste ella pestis* were injected intraperitoneally into mice t virulent strain acquired the ability to resist phagocyto by mouse polymorphonuclear cells whereas the avirule strain did not; the development of this resistance phagocytosis was found in strains in which there was visible capsulation. Strains possessing this property we shown, by the agar gel diffusion precipitation techniq to have 2 additional antigens, designated V and W; o has not been found without the other. Thus all high virulent strains of *P. pestis* are capable of producing n only fraction 1 antigen but also the antigens V and

Applying the above experience to the examination o number of laboratory strains of *P. pseudotuberculosis* was not possible to detect the production of any V or antigens. When, however, freshly isolated strains fr natural infections were examined the production of V a W antigens was a frequent finding. Of 38 recently iso ted strains it was possible, by colony selection, to obt cultures from 27 that were VW+ (that is to say, they p duced V and W antigens). Cultures maintained and p pagated at temperatures not exceeding 28°C. showed gross population changes, but repeated subculture 37°C. resulted in selective elimination of VW+ org nisms. VW− strains of *P. pseudotuberculosis* are mu less virulent for mice as compared with their VW counterparts. *H. J. Benstea*

FERNELIUS, A. L., DEARMON, I. A., Jr., KLEIN, F. LINCOLN, R. E. **Comparison of Graded a Quantal Virulence Tests for *Bacillus anthra* Spores.** *J. Bacteriology.* 1960, Apr., v. 79, No. 594–600, 3 figs.

"The virulence of spores of four strains or variants *Bacillus anthracis* with characteristics of high virule and four with low virulence were compared in mice both an LD_{50} and a median-time-to-death method. B intraperitoneal and subcutaneous routes of challenge w employed and compared. There was good correlat between the LD_{50} and the median-time-to-death vall for all strains or variants tested by both routes. Wit *anthracis* of high virulence, a greater number of spo was required to produce death by the intraperiton route than was required by the subcutaneous route. H ever, by the median-time-to-death method of measur virulence, the intraperitoneal route killed mice soo indicating an increased virulence over that given by subcutaneous route. This fact held true for high c centrations of spores with characteristics of high and virulence. However, when spores of low virulence w diluted 100-fold, and injected by the subcutaneous ro shorter median-time-to-death values resulted."

STANLEY, J. L., SARGEANT, K. & SMITH, H. **Purification of Factors I and II of the Anthrax Toxin produced** *in vivo*. *J. General Microbiol.* 1960, Feb., v. 22, No. 1, 206–18, 1 pl. [12 refs.]

"Highly labile factors (I and II) of anthrax toxin were purified from the toxic plasma of guineapigs just dead from anthrax by fractionation methods which involved the minimum of inactivation. The final preparations of factors I and II, which still contained constituents of guineapig plasma, were toxic when injected together but innocuous when injected separately."

SARGEANT, K., STANLEY, J. L. & SMITH, H. **The Serological Relationship between Purified Preparations of Factors I and II of the Anthrax Toxin produced** *in vivo* **and** *in vitro*. *J. General Microbiol.* 1960, Feb., v. 22, No. 1, 219–28, 3 figs. [15 refs.]

"A serological comparison on gel-diffusion plates of purified preparations of factors I and II of the anthrax toxin obtained *in vitro* and *in vivo* indicated that all but one (factor I from *in vitro* sources) of these preparations contained at least two major serological components. At least three serological components were involved in the total system: A (associated with factor I activity); B (associated with factor II activity); C (not associated with toxic activity). These results indicated that no preparation of factor II of the anthrax toxin so far examined was immunologically homogenous and that the serological connexion between factor I of the anthrax toxin (produced *in vivo*) and the protective factor produced *in vitro* (Smith, 1958) was due to a common component not associated with factor I activity. There was some evidence that the method of measuring immunogenicity in certain culture filtrates of *Bacillus anthracis* by serological precipitation (Thorne and Belton, 1957) is not generally applicable to all products of this organism."

MOMOSE, H. & IKEDA, Y. **Isolation of Mutants of** *Bacillis subtilis* **requiring D-Glutamic Acid.** [Correspondence.] *Nature*. 1960, May 14, v. 186, 567–8, 1 fig.

STÜMPEL, K. Ist bei der aktiven Immunisierung gegen Tetanus ein sicherer Impfschutz zu erwarten, wenn die Zweit-Impfung später als 12 Wochen nach der Erst-Impfung erfolgt? [**Is Satisfactory Active Immunization against Tetanus obtained if more than 12 weeks elapse between the First and Second Inoculations?**] *Zent. f. Arbeitsmed. u. Arbeitsschutz*. 1960, Mar., v. 10, No. 3, 53–4.

The question which is the title of this paper is important since various circumstances may prevent the second inoculation against tetanus being given until several months after the first. No definite answer to the question could be obtained from the literature or from the manufacturers of the active immunization material (Tetanol). This paper describes the results, recorded in a detailed table, obtained with miners whose second injection was not given until 9 to 15 months after the first. The total number of miners at the beginning of the investigation was 25 but of these 5 did not appear for the second inoculation and 1 was found to have a high titre of antitoxin before the second injection. In the remaining 19 men all had developed the satisfactory antitoxin titre of 0·02 units or more after the second injection. The practical value of this finding is shortly discussed although it is realized that the number of cases in this enquiry was small. *M. E. Delafield*

BONVENTRE, P. F. & KEMPE, L. L. **Physiology of Toxin Production by** *Clostridium botulinum* **Types A and B. I. Growth, Autolysis, and Toxin Production.** *J. Bacteriology*. 1960, Jan., v. 79, No. 1, 18–23, 4 figs. [14 refs.] **IV. Activation of the Toxin.** *Ibid.*, 24–32, 3 figs. [17 refs.]

I. "The normal growth cycle of the strains of *Clostridium botulinum* studied was found to be characterized by a period of cell multiplication immediately followed by active autolysis of the cells which continued until few viable organisms remained. Autolysis was established as an important mechanism for the liberation of the toxin. This was based upon two observations; first, that the toxicity of culture filtrates was not correlated with the number of intact organisms, but rather with the degree of autolysis of the cultures; and second, that artificial disruption of cultures at the end of the logarithmic growth phase resulted in the liberation of large quantities of intracellular toxin. The inability to obtain nontoxic wash fluids from intact cells and the low level of toxicity observed in young culture filtrates were attributed to simple diffusion of the toxin.

IV. "The potential toxicity of cultures of *Clostridium botulinum* in the exponential growth phase was found to be much greater than their apparent toxicity. The increases in toxicity noted during the period of cellular degeneration could not be attributed to protein synthesis *de novo* since this increase was noted in the presence of chloramphenicol, an effective inhibitor of protein synthesis. Furthermore, no increases in total protein could be demonstrated during autolysis. It was concluded that the toxins of *C. botulinum* types A and B are initially synthesized as large molecules with comparatively low biological activity owing to masking of active chemical groupings. These toxin 'precursors' must be partially degraded, probably by the proteolytic enzymes of the organisms before manifesting their full toxic potentialities."

[Parts II and III will be abstracted in the September issue of this *Bulletin*.]

SIEFERT, G. Experimentelle Untersuchungen über Spirochäten-Antigene. III. Mitteilung. Serologische Analyse der aus *Treponema pallidum* isolierten Lipoid- und Eiweissfraktionen. [**Investigations on Spirochaetal Antigens. 3rd Communication: Serological Analysis of Lipid and Protein Fractions isolated from** *Treponema pallidum*] *Ztschr. f. Immunitätsf. u. Exper Therap.* 1960, Jan., v. 119, No. 1, 120–30, 2 figs. [14 refs.]

An extract of Nichols strain treponemata was prepared on a large scale from 300 syphilitic rabbit testicles and this was used for a wide range of experiments on separation of fractions by the technique of paper electrophoresis. These fractions were then examined in respect of their power of giving complement absorption with syphilitic serum and of absorbing the different antibodies from such sera.

It was possible to distinguish 5 protein and 2 lipid components in the extract. One of the lipid elements coincided with the protein component No. 4 and a protein-lipid complex may be the active substance. On comparing observations of the strength of these different components and a variety of recognized antigens the order of potency found was Pallida Ext. (product of firm Meinicke of Munich)>Fraction IV (lipo-protein)>complete extract>, Fraction I>cardiolipin.

The observations on absorption were not very convincing. The serum was exposed to the various antigens already absorbed on Kaolin.

The reagin, *i.e.* antibody reacting with lipoid antige was the only one completely absorbed and the only su cess in absorbing the antibodies reacting with the prote antigens was obtained with a preparation of Reiter spir chaetes freed from lipoid. Observations on heat liabili showed the protein antigens to be destroyed at 56° whereas the lipoid antigens resisted 30 minutes, heating 70°C. [See also this *Bulletin*, 1960, v. 35, 149.]

J. W. McLeod

Brzin, B. & Vargazon, N. Listerioza pri človek **[Listeriosis in Man]** *Zdravstveni Vestnik*. Ljubljan 1960, v. 29, Nos. 1/2, 1–8, 7 figs. & 1 diagram. [refs.] English summary.

The organism was isolated from purulent cerebrospin fluid of a boy aged 13 months. [See also this *Bullet.* 1957, v. 32, 625.]

RICKETTSIAE

Kohno, S. **Studies on Metabolism of Rickettsia. I. Studies on Dehydrogenases of** *Rickettsia mooseri*. *Japanese J. Med. Sci. & Biol.* 1959, Oct., v. 12, No. 5, 375–85, 2 figs. [16 refs.]

Fujita, K., Kohno, S. & Shishido, A. **The Incorporation of Methionine into Purified Rickettsiae.** *Japanese J. Med. Sci. & Biol.* 1959, Oct., v. 12, No. 5, 387–90, 2 figs.

Bell, E. J. & Stoenner, H. G. **Immunologic Relationships among the Spotted Fever Group of Rickettsias determined by Toxin Neutralization Tests in Mice with Convalescent Animal Serums.** *J. Immunology*. 1960, Feb., v. 84, No. 2, 171–82. [refs.]

[An abstract of this paper appeared in the *Tropica Diseases Bulletin*, 1960, v. 57, 800.]

Golinevitch, Hélène. A propos de la différenciation quelques rickettsies du groupe de la fièvre pourpr à tiques. **[Differentiation of Some Rickettsiae the Tick Typhus Group]** *Arch. Inst. Pasteur Tunis*. 1960, Mar., v. 37, No. 1, 13–22.

[An abstract of this paper appeared in the *Tropica Diseases Bulletin*, 1960, v. 57, 800.]

BACTERIOPHAGES

Epstein, H. T. **Studies of Phage Growth in Irradiated Cells.** *Arch. Biochemistry*. 1960, Feb., v. 86, No. 2, 286–93, 6 figs. [23 refs.]

From experiments in which *Escherichia coli* B cells were irradiated with UV light or X-rays before infection with T2, the number of hits required to destroy the capacity of the cells to support phage multiplication was calculated. Similarly, from experiments in which phage-infected bacterial complexes were exposed to different UV doses during the latent period, the number of hits required to destroy the phage being synthesized was calculated. The latter type of experiment had been interpreted to indicate that phage particles are synthesized separate cellular centres [Epstein, *Bull Math. Biophy* 1956, v. 18, 265], and it appears that the number of th per cell is equivalent to the number of targets per c deduced from capacity curves. Irradiation of the ce before infection and after infection reduced the numl of targets and the number of cellular centres by the sa factor. This was confirmed with *Pseudomonas pyo anea* and its phage p8, and also with lysogenic cells.

Survival curves drawn for *E. coli* B cells infected w T2 and irradiated with UV light of wavelengths 260 a 280mμ at intervals during the latent period showed th the light-absorbing properties of the materials controll

age synthesis did not change during the course of age development. Thus it seems likely that the cellular ntres, like the materials initiating phage synthesis, are cleic acid, and that they are related to structures exist- g in the cell before infection. These may be the nuclear odies. *Janice Taverne*

STRACHAN, L. & VOLKIN, E. **Properties of Ribonucleic Acid Turnover in T2-Infected** *Escherichia coli*. *Biochim. et Biophys. Acta.* 1958, Sept., v. 29, No. 3, 536–44, 5 figs. [14 refs.]

ANTOS, Judith, VARGA, I. & IVÁNOVICS, G. **Characterization of Anthrax Phages.** *Acta Microbiologica.* Budapest. 1960, v. 7, No. 1, 31–42, 4 figs. [13 refs.]

8 strains of phage isolated from soil and specific for *Bacillus anthracis* were antigenically of 2 kinds, while the anthrax phage W and its mutants isolated by MCCLOY from a lysogenic *B. cereus* [this *Bulletin,* 1958, v. 33, 707] differed from both. Within these 3 antigenically separate groups, the phages formed similar plaques and were equally sensitive to citrate, heat and UV light.

Experiments on virulence did not give clear cut results. Some of the phages appeared to lysogenize bacteria and to be carried as prophage in spores subsequently formed, but the condition was unstable and no persistently lysogenic cells were obtained. *Janice Taverne*

VIRUSES

The order in this section is:—**General; Psittacosis-Lymphogranuloma group; Pox group; Respiratory group; Reovirus group; Enteric group; Arthropod-borne group; Others.**

ERGMAN, S., NILSSON, S. B. & OLSSON, S. G. **Two Established Human Cell Lines: Cultivation and Susceptibility to Viruses.** *Acta Path. et Microb. Scandinavica.* 1959, v. 47, No. 4, 387–92, 3 figs.

The establishment of 2 continuous cell lines from uman tissues is described and illustrated. One was erived from human amnion and the other from a foetal arotid gland. The human amnion cells were sensitive the following virus types: poliovirus 1, 2 and 3, ECHO 2, 9 but not ECHO 3, 11 or adenovirus 2 and 4. The arotid cells were sensitive to all these viruses except CHO 11 and adenovirus 4. The virus titres in the cell nes were similar to those obtained in HeLa or primary uman amnion or kidney cells. *A. J. Beale*

ALDUCCI, D., ANDREONI, G., GORI, G. B., CASTELLI, L. & MANCINI, G. **Cytopathic Index: A New Method for the Quantitative Evaluation of Tissue Culture Infectivity of Different Virus Strains.** *J. Bacteriology.* 1960, Mar., v. 79, No. 3, 379–83, 4 figs. [12 refs.]

The 50% infectivity endpoint titre of virus grown in ssue culture (TCD50) does not completely identify the rowth characteristics of a strain. One facet which is ormally neglected is the rate of development of cyto- athic effects. Thus, if daily readings of the titre are nade, the pattern produced by different viruses on a iven cell type differs as does that of the same virus on ifferent cells. A mathematical expression of these differ- nces, referred to as the cytopathic index, is proposed nd is suggested as a useful marker characteristic for dentifying virus strains. *A. J. Beale*

BAUER, D. J. **Some Applications of a Single-Dilution Method of Titrating Neurotropic Viruses in Zero Mortality (D_0) Units.** *Brit. J. Exper. Path.* 1960, Apr., v. 41, No. 2, 130–39, 6 figs.

Using neurovaccinia virus inoculated intracerebrally in 10-fold dilutions into mice the author found a rectilinear relation between log dose and the reciprocal of the survival time, deaths being recorded twice daily [see also this *Bulletin,* 1959, v. 34, 290]. This straight line cuts the abcissa at a log dilution of virus which represents the LD0 (the lowest dilution killing no mice) which may be called the D_0. The slope of the line was found to have a standard error of 14%. In 3 separate replicate titrations the D_0 was found to be 7·9, 7·9 and 7·8 log and the LD50 6·0, 6·3 and 6·0—the mean difference was 1.65 log so that the LD50 of this virus may be derived as 40 D_0.

Similar rectilinear response curves with slopes with standard errors of 5–31% were demonstrated for ectromelia, 17D yellow fever and herpes simplex and slopes are given for 4 other viruses.

The titre of a preparation can be calculated in D_0 by inoculation of a single dilution into a group of mice: the mean reciprocal survival time divided by the slope previously determined for the particular virus gives the D_0 in log units. With multiple dilutions the slope can be derived in the actual experiment. The use of single dilution titrations by the D_0 method in antiviral chemotherapy trials, determination of growth curves, investigation of the kinetics of virus inactivation and in neutralization tests [see also SMITH and WESTGARTH, this *Bulletin,* 1959, v. 34, 1304] is discussed. The main advantage of the method is that each n animals used can yield $n(2t + 1)$ responses where t is the survival time, compared with only $n + 1$ responses where only death or survival are considered (quantal response). The latter method sacrifices all the information about t.

C. E. Gordon Smith

García Gancedo, A. & Sierra, G. Action *in vitro* de la fénacine alfa-carboxylamide sur les virus encéphalitique équin ouest, poliomyelitique, fixe de la rage et vaccinal. [**Action *in vitro* of Fenacine Alpha-Carboxylamide on the Viruses of Western Equine Encephalomyelitis, Poliomyelitis, Rabies and Vaccinia**] *Antonie van Leeuwenhoek: J. Microbiol. & Serol.* 1959, v. 25, No. 3, 349–52.

"Fenacine alpha-carboxylamide" is a substance with an anti-fungal action obtained by one of these authors (Sierra and Veringa, *Nature,* 1958, v. 182, 265: in this paper the substance is called "oxy-chloraphin") from submerged cultures of *Pseudomonas pyocyanea.* By what process of reasoning the authors came to testing its action on viruses is not explained.

The facts reported here are that when 200 LD50 of Western equine encephalomyelitis virus in the form of mouse brain suspension are mixed with an equal volume of 1% suspension of this substance and kept at 4°C. for 5 hours, intracerebral inoculation of mice with one half of this mixture (*i.e.,* 100 LD50) has no effect, whereas controls inoculated with virus + saline all die. Mice surviving the medicated inoculum succumb to subsequent inoculation with untreated virus. Similar tests with the viruses of poliomyelitis, rabies and vaccinia revealed no activity whatever against these viruses. [The numbers of mice in the "groups" used are not stated.]

L. P. Garrod

Hurst, E. W. & Reeve, P. **Transmission of the Viruses of Trachoma, Inclusion Blennorrhoea and Lymphogranuloma to Mice.** [Correspondence.] *Nature.* 1960, Apr. 23, v. 186, 336.

This note reports the successful transmission of some strains of trachoma and inclusion blenorrhoea intracerebrally in mice. Animals 5 weeks old of the BSVS strain of Webster proved most suitable. With the Tang strain of trachoma 4 series of passages initiated with infected yolk-sac material have been successful; this was not facilitated by cortisone. Failure is recorded with 2 other strains; G1 and G17. Symptoms of disease—ruffled fur, hunched posture and stilted gait—became evident after 3–4 passages; they had their onset 3–4 days after infection. Some of the mice also developed purulent conjunctivitis. Infective mouse brain material (17th passage) failed to produce disease in a macaque monkey on intracerebral inoculation and evoked no reaction when rubbed into the scarified conjunctiva of the upper tarsus in another monkey. Group antigen of the psittacosis-lymphogranuloma viruses was demonstrated in the infective mouse brain by complement fixation but no virus particles could be seen in preparations stained by appropriate methods nor could virus particles be demonstrated by differential centrifugation. However, injection of this material into the yolk-sac of developing chick embryos evoked production of typical virus particles. One of two strains of inclusion blenorrhoea virus were similarly established in mouse brain, as were two strains of lymphogranuloma virus. Passage of normal mouse brain failed to produce disease and cultural tests excluded bacteria as a cause.

S. P. Bedson

McCarthy, K. & Helbert, D. **A Comparison of Haemagglutinins of Variola, Alastrim, Vaccinia, Cowpox and Ectromelia Viruses.** *J. Path. Bact.* 1960, Apr., v. 79, No. 2, 416–20. [20 refs.]

The pox viruses tested all behaved very similarly in haemagglutination and haemagglutination-inhibition tests. The viruses could be distinguished neither by haemagglutination inhibition nor by differences in agglutinating activity against red cells from several species. Cells from 12 out of 15 mature fowls reacted with the haemagglutinins. Chick embryo cells did not react but a month after hatching the cells of 2 out of 4 of these chicks were agglutinable. Mouse red cells were uniformly sensitive except to cowpox agglutinin. Cow red cells were insensitive, as were human cells. 3 out samples from pigeons were weakly agglutinable.

Colin Kaplan

Hanafusa, T.; Hanafusa, H.; Kamahora, J. **Transformation Phenomena in the Pox Group Viruses. I. Transformation of Ectromelia into Vaccinia Virus in Tissue Culture** [Hanafusa, T., Hanafusa, H. & Kamahora]. *Biken's J.* Osaka. 1959, Aug., v. 2, No. 2, 77–84, 3 figs. [11 refs.] **II. Transformation between Several Members of Pox Group** [Hanafusa, H., Hanafusa, T. & Kamahora]. *Ibid.,* 85–91. [12 refs.]

I. Monolayer cultures of L cells were inoculated with mixtures of active ectromelia virus and heat-killed vaccinia virus, and 48 hours later active vaccinia virus was recovered. Ectromelia and vaccinia virus may be distinguished by differences in animal pathogenicity, heat stability, cytopathogenesis in tissue cultures and plaque size. The virus recovered from the cultures had the characteristics of vaccinia virus, and was stable after passages at limiting dilution. Transformation was demonstrated when the heat-killed vaccinia virus was added to L cell cultures 24 hours before the active ectromelia virus. It was also shown to occur in cultures of HeLa cells, human amnion cells and in the chick embryo chorio-allantoic membrane.

II. Using fibroma, myxoma, fowlpox, ectromelia and 2 strains of vaccinia viruses the authors demonstrated transformation within the pox group of viruses. With poliomyelitis, influenza and measles viruses were used as the active part of a system, transformation did not occur. Transformation would only occur in cells which supported the multiplication of both viruses: attempts at transformation involving myxoma virus failed in cells in which myxoma virus will not grow. [See also *Bulletin,* 1960, v. 35, 87.]

Colin Kaplan

Mahnel, H. & Munz, E. Differenzierung von Variola- und Vakzinevirus in HeLa- und Fl-Zellkultur. Ein Beitrag zur Varioladiagnose. [**Differentiation of Variola and Vaccinia Virus in HeLa and Fl Cell Cultures**] *Zent. f. Bakt.* I. Abt. Orig. 1959, v. 178, No. 2, 149–55, 6 figs.

AUER, D. J. & SADLER, P. W. **New Antiviral Chemotherapeutic Agent active against Smallpox Infection.** *Lancet.* 1960, May 21, 1110–11.

This short paper reports experimental results of great interest. N-ethylisatin β-thiosemicarbazone administered to mice up to 6 hours after intracerebral infection with Rastrim virus protected them from encephalitis and death. The drug has a low toxicity and was active at a dose of 5 mgm. per kgm. *Colin Kaplan*

WOODROOFE, Gwendolyn M. **The Heat Inactivation of Vaccinia Virus.** [Correspondence.] *Virology.* New York. 1960, Mar., v. 10, No. 3, 379–82, 2 figs.

The author of this letter reports experiments which showed that freshly extracted suspensions of vaccinia virus or suspensions frozen at −60°C. immediately after preparation were inactivated according to first-order kinetics when heated at temperatures of 50°C. or more. Virus stored at 4°C. for 1 day or longer developed a non-genetic heat-resistant fraction like that described recently by KAPLAN [this *Bulletin*, 1958, v. 33, 993].

Colin Kaplan

WIGAND, R. Über die antikomplementäre Aktivität von Antigenen aus normalen und mit Vaccinevirus infizierten HeLa-Zellkulturen. [**The Anti-complementary Activity of Antigens from Normal HeLa Cell Cultures and Cultures Infected with Vaccinia Virus**] *Arch. f.d. gesamte Virusforschung.* 1960, v. 10, No. 1, 139–49, 1 fig. [11 refs.]

The English summary appended to the paper is as follows:—

"The anticomplementary activity of antigens from normal HeLa cell cultures, and cultures infected with vaccinia virus, has been investigated.

"Culture fluid of normal HeLa cells after incubation in a serum-free maintenance medium showed anticomplementary activity. It was destroyed by heating to 62°C.; it could be removed by extraction with fluorocarbon; and it was inhibited by heated normal serum. The occurrence of this inhibitor in sera was dependent on the species and individuality of the animal. It was found in all guineapig sera, in most rabbit sera, and in some horse sera. The inhibitor was partially inactivated by heating for 30 minutes to 60°C., and completely at 64°C. In HeLa cultures infected with vaccinia virus, an anticomplementary factor was found, even in the presence of serum, which differed from that found in normal cultures by its greater thermostability. It was not present in cultures infected with adenovirus type 3 or ECHO 6-virus. The cellular moiety of all cultures was devoid of anticomplementary activity."

FISEK, N. H. **Kinetics of Deterioration of Smallpox Vaccine.** *Bull. World Health Organization.* Geneva. 1960, v. 22, Nos. 3/4, 435–7, 2 figs.

FALKE, D., SIEGERT, R. & VOGELL, W. Elektronenmikroskopische Befunde zur Frage der Doppelmembranbildung des Herpes-simplex-Virus. [**Electron Microscope Findings on the Question of the Formation of the Double Membrane of Herpes Simplex Virus**] *Arch. f.d. gesamte Virusforschung.* 1959, v. 9, No. 4, 484–96, 9 figs. (8 on 6 pls.). [10 refs.]

The authors have studied the development of the Lennette strain of herpes virus in HeLa cells by the examination of ultrathin sections in the electron microscope. The nuclei of infected cells showed margination of the chromatin, and contained many incomplete virus particles lacking an outer double membrane, together with a number of large inclusions which contained incomplete virus particles 110 mμ in diameter and also complete particles with double membranes 150–170 mμ in diameter. The periphery of the nuclei also contained structures adjacent to the marginal chromatin resembling threads, tubes and islets, which were filled with incomplete particles, and consisted of invaginations of the inner lamella of the nuclear membrane, the outer lamella of which showed a corresponding dilation passing into the cytoplasm. The invaginations contained numerous thread-like structures which were extended or coiled spirally, which were apparently processes of the inner lamella and thus in communication with the nuclear contents. The appearances suggested that the complete virus particles were formed by the detachment of segments of the thread-like structures. *D. J. Bauer*

SHUBLADZE, A. K. & KHUAN, Chzhu-Shan. **Study of the Antigenic Properties of Herpes Virus.** *Problems of Virology.* London. 1959, v. 4, No. 1, 78–83. [10 refs.] [Translated from Russian.]

Skin tests were performed by inoculating into the forearm a formolized suspension of mouse brain infected with herpes simplex virus. Uninfected mouse brain was used as a control. 80% of 106 subjects with a history of herpes infection and 32% of 103 with no history of infection gave positive reactions. The authors claim that the test will be of value in diagnosis, provided a polyvalent antigen is used. They argue that the virus was latent in those giving positive reactions with no evidence of infection, and that no reaction was obtained in 20% of those with a history of infection because the strain of virus employed was antigenically different from the one causing infection. They found that the results of neutralization tests in mice with 7 strains of virus isolated from patients indicated that the strains belonged to 3 antigenically distinct groups and complement-fixation tests are reported to support this.

[Insufficient serological details are given for the reader to judge for himself the value of the skin test or the extent of the differences between virus strains.]

Janice Taverne

ISHIDA, N.; MIZUNO, H.; CHIBA, A.; NAKAZIMA, S.; KOSAKA, Y.; SASAKI, Y.; SASAKI, H. **Studies on Experimental Influenza in Mice. I. Virus Growth and Immune Response in Mice when the Inoculum was given from Three Different Routes** [ISHIDA, MIZUNO, CHIBA & NAKAZIMA]. *Tohoku J. Exper Med.* 1959, Dec., 25, v. 71, No. 2, 137–50, 6 figs. [11 refs.] **II. Absolute Amount of Virus introduced into the Respiratory Tract of Mice by Standard Inhalation Procedure** [ISHIDA, KOSAKA & SASAKI, Y.]. *Ibid.*, 151–61, 1 fig. [11 refs.] **III. Early Distribution of P^{32} Labeled Virus in Organs of Mice after Administration from Three Different Routes** [ISHIDA, KOSAKA & SASAKI, H.]. *Ibid.*, 163–70, 2 figs.

I. Influenza A (PR8) virus was inoculated into 3-week-old mice by the intranasal (inhalation), intracerebral and intraperitoneal routes and the infectivity and haemagglutination titres reached in lung, liver, spleen and kidney tissues were estimated at 1, 3 and 5 days after inoculation. Lung tissue showed the highest virus content irrespective of the inoculation route, reaching comparable titres at the third day of infection and subsequently falling off in animals inoculated intraperitoneally or intracerebrally but not in those inoculated intranasally. This drop in titre was correlated with development of antibodies and resistance to virus challenge.

II. Comparative titrations of influenza viruses were carried out in mice inoculated intranasally either by instillation or by inhalation. The first method gave 50% endpoints approximately 10 times higher than the second. A further difference between the 2 methods was manifested by the higher slopes of dose-response curves in titrations performed by inhalation. Using virus labelled with ^{32}P the authors estimated that about 50% of the virus inoculated by instillation was localized in the respiratory tract, whereas the corresponding figure for mice inoculated by inhalation was considerably smaller.

III. Mice were inoculated by the intranasal (instillation), intracerebral and intraperitoneal routes with influenza virus labelled with ^{32}P and the distribution of radioactivity in various organs was determined 30 minutes and 3 hours later. After intracerebral inoculation, radioactivity was mainly detected in brain and liver, whereas after intranasal inoculation most of the radioactivity was found in the lungs, and after intraperitoneal inoculation relatively low activity was detected in liver, kidney and spleen. Radioactivity measured in the various organs at 3 hours was slightly lower than at 30 minutes except in the mice inoculated intraperitoneally, where the reverse was the case.

Radioactivity in the blood from mice inoculated intranasally showed a sharp rise at 4 hours and it is suggested that this may have been due to breakdown of virus particles. *H. G. Pereira*

LIPPELT, H. & WIRTH, W. Unspezifische Hemmfaktoren im Meerschweinchen-Normal-Serum gegenüber Influenza-Viren. [**Unspecific Inhibitors of Influenza Viruses in Normal Guineapig Serum**] *Arch. f.d. gesamte Virusforschung.* 1959, v. 9, No. 4, 497–509. [60 refs.]

In the typing by means of haemagglutination-inhibit tests of 7 strains of A2 influenza virus isolated in Germa during the epidemic of 1957–58 it was found that 5 stra were inhibited unspecifically to high titres. A furt investigation of this phenomenon was carried out w normal sera in comparison with reference strains of ty A, A prime and B virus; unspecific inhibitor was not p sent in chick and mouse sera, but was found in rabbit a ferret sera, and in particularly high titres in guinea serum. The inhibition titre observed in the latter c with 4 strains (2560) was higher than that obtained w heated Lee virus (640), and showed a 2–4 fold incre when the guineapig serum was heated at 56°C. for minutes; a titre of 10,240 was obtained when the heat was carried out at 62°C., and 40,960 at 70°C. T increase of titre was not seen with the Lee strain. T unspecific inhibitor of guineapig serum was largely d troyed by treatment with trypsin, and could be partia removed by adsorption on to kaolin. Infectivity titrat carried out in eggs with one of the strains showed tha was unspecifically neutralized by normal guineapig seru The results thus show that the inhibitor present guineapig serum differs from the Francis and Chu inhi tors in a number of respects, and the authors consi that it may be identical with the β-inhibitor of SM and WESTWOOD [this *Bulletin*, 1949, v. 24, 910]. *D. J. Baue*

MELANDER, B. **N^1,N^1-Anhydrobis-(β-Hydroxyeth biguanide-Hydrochloride (ABOB) in Prophyla and Suppression of Experimental Influen** *Antibiotics & Chemotherapy.* New York. 19 Jan., v. 10, No. 1, 34–45, 2 figs. [42 refs.]

ABOB (see title) is one of a series of biguanides wh have been examined for activity against influenza vi Mice were inoculated with mouse-adapted PR8 or I virus by exposure in a chamber to nebulized virus s pension, and treated with the drug by subcutaneous jection. They were killed 3 or 4 days later if not alre dead, and the degree of pulmonary consolidation v scored as 25, 50, 75 or 100%. Assessment of the resu is based on these scores in groups of mice. To obtain effect it was necessary to start medication before ino lation (in some experiments doses were given 48, 24 a 3 hours beforehand) and the results were improved also administering "xerostomia-producing" [*i.e.*, at pine-like] drugs. 2 of these were used in different do Some mice were also given ammonia inhalation bef hand to increase their susceptibility. A table occupy 3 whole pages gives the results of these rather com cated experiments. [They are not impressive, but sc are said to be significant.] *L. P. Garro*

SQUERI, L. & PERNICE, A. La reazione di "emoaggl nazione indotta" per la ricerca degli anticorpi gli adenovirus. [**The Induced Haemagglutinat Reaction in the Detection of Adenovirus An bodies**] *Giorn. di Batteriol., Virol. ed Immun* 1959, July–Oct., v. 52, Nos. 7/10, 299–308. Eng summary (8 lines).

An investigation has been made of the use of the duced haemagglutination reaction for the demonstrat

adenovirus antibody. A 4% suspension of sheep red ls was treated with an equal volume of a 1:20,000 ution of tannic acid in saline for 30 minutes at 20–°C. and then washed 3 times in saline and resuspended a concentration of 2%. The tanned cells were then nsitized by contact for 30 minutes at 20–25°C. with igen consisting of dialysed fluid from HeLa cell cul-es infected with types 1, 3, 5 or 9 adenovirus. The t was carried out by mixing the prepared cells with utions of serum: after standing for 2–4 hours at room nperature the presence of antibody was indicated by occurrence of haemagglutination. Types 1 and 5 anti-a gave similar titres (256–1024) with the 4 types of igen, and the reaction is therefore not type-specific. e sera of 48 healthy residents of Messina aged 16–55 ars were examined in parallel by the induced haemag-tination and complement-fixation tests; positive results re obtained in 40 (83·3%) by the complement-fixation d in 34 (70·8%) by the induced haemagglutination test.

D. J. Bauer

RDAN, W. S., Jr. **Stability Characteristics of Coe Virus.** *Proc. Soc. Exper. Biol. & Med.* 1960, Mar., v. 103, No. 3, 506–9, 3 figs.

The resistance of Coe virus [LENNETTE *et al.*, this *lletin*, 1959, v. 34, 397] to various physical and chemi-treatments was investigated. Viral infectivity was pre-ved for relatively long periods of storage at −70°C., 4°C. or room temperature. At 37°C. infectivity titres pped to 10% of the original within 2 days and to less n 1% at 20 days. At 50°C. most of the infectivity was t by 30 minutes. The virus resisted repeated cycles of ezing and thawing, was stable at *p*H 6 to 9 and resisted er treatment. [See also PEREIRA and PEREIRA, *Ibid.*, 60, v. 35, 90.] *H. G. Pereira*

NKOVICS, J. **Interactions of the Newcastle Disease Virus with Mouse Tissues. I. Enhancement of the Neurotoxicity of the Virus and Preliminary Experiments with Toxic Brain Extracts.** *Arch. f.d. gesamte Virusforschung.* 1960, v. 10, No. 1, 103–25, 7 figs. [14 refs.]

ROUHET, Victoria, with the technical collaboration of H. GOAREGUER. Lésions cellulaires provoquées par les réovirus (virus ECHO 10). Anticorps fluores-cents et étude cytochimique. [**Cellular Lesions induced by Reovirus (ECHO 10). Fluorescent Antibody and Cytochemical Studies**] *Ann. Inst. Pasteur.* 1960, Apr., v. 98, No. 4, 618–21, 6 figs. on pl. [10 refs.]

The development of the inclusion body in monkey dney cultures infected with the Lang prototype strain type 1 Reoviruses [formerly ECHO 10, see this *Bulle-n*, 1960, v. 35, 514] was followed by means of Coons' uorescent antibody technique. It was found that viral ntigen appeared in the cytoplasm and had the shape nd position characteristic of the inclusion bodies. These odies stain positively for ribonucleic acid. From these 2 pieces of evidence it is concluded that the inclusion in Reovirus infected cells is virus. *A. J. Beale*

HORNE, R. W. & NAGINGTON, J. **Electron Microscope Studies of the Development and Structure of Poliomyelitis Virus.** *J. Molecular Biol.* London. 1959, Dec., v. 1, Nos. 4/5, 333–8, 1 fig. & 7 pls. [20 refs.]

In 1959 FINCH and KLUG, by X-ray diffraction, found the diameter of individual poliomyelitis virus particles to be approximately 300 Å [this *Bulletin*, 1959, v. 34, 1192]; previous workers, among whom are SABIN *et al.* [*ibid.*, 1954, v. 29, 886], SCHWERDT *et al.* [*Ibid.*, 1201] and SJÖSTRAND and POLSON (1958), had given estimations between 220 Å and 310 Å. The size and symmetry of the particles as seen by X-ray diffraction were similar to those of turnip yellow mosaic virus recorded by COSSLETT and MARKHAM (1948) and others.

The authors of this paper compare these results with their own from a time interval study of HeLa cell mono-layers infected with 3 classical strains of poliovirus. Fragments of the infected cells, negatively stained by the technique of HORNE and BRENNER (1958) and sprayed on-to carbon grids, were used to obtain high resolution elec-tron micrographs of viable poliovirus particles at various stages in the elaboration cycle. Avoidance of atmospheric contamination during the process of spraying was achieved by using the apparatus which is figured.

The 7 plates to which reference is made show stages in the assembly of virus particles from subunits within a containing membrane. 3 kinds of particles were iden-tified—complete, incomplete and empty shells. Measure-ments relating to the unfixed virus are given and the development and structure of the virus discussed.

R. G. Bird

THOMSSEN, R., HAAS, R., DOSTAL, V. & RUSCHMANN, E. Über den Einfluss des Beimpfungsvolumens auf die Adsorption von Poliomyelitisvirus an Gewebekul-turen. [**The Effect of the Volume of the Inocula-tion upon the Adsorption of Poliomyelitis Virus on to Tissue Cultures**] *Ztschr. f. Hyg. u. Infek-tionskr.* 1959, v. 146, No. 2, 114–22, 2 figs. [14 refs.]

An investigation has been made of the effect of the volume of the inoculum upon the rate of adsorption of the Mahoney strain of type I poliomyelitis virus onto cultures of trypsinized rhesus monkey kidney cells. Virus in a dose of 78 plaque-forming units was added to cell monolayers in volumes ranging from 0·1 to 10 cc. After varying periods from 15 to 120 minutes the inoculum was withdrawn, the cell sheet was washed and overlaid with agar, and the plaques which developed during subsequent incubation for 6 days were counted. With an inoculum of 1 cc. 40 plaque-forming units became adsorbed after 120 minutes, compared with less than 10 with an inoculum of 10 cc. In a similar experiment with a constant adsorp-tion period of 120 minutes 100% adsorption was obtained with an inoculum of 0·1 cc. and 18·2% with an inoculum of 5 cc. A similar effect could also be demonstrated in roller tube cultures. *D. J. Bauer*

WECKER, E. **A Simple Test for Serodifferentiation of Poliovirus Strains within the same Type.** [Correspondence.] *Virology*. New York. 1960, Mar., v. 10, No. 3, 376–9. [10 refs.]

A method of measuring antigenic differences within the main serological types of poliovirus is described. Virus is allowed to adsorb to cell monolayers which are then overlaid with specific immune serum. The mean diameter of plaques is then measured and expressed as a percentage of their diameter in control plates free from antiserum. This method is a rapid screening method for analysing serological variants and can be used not only with intact virus but also infectious RNA since it is the progeny virus antigenic structure that influences plaque size. It is stressed that antiserum to plaque-purified virus must be used and that perfect cell sheets are needed to minimize variations in plaque size on a plate or between plates. *A. J. Beale*

KOPROWSKI, H., NORTON, T. W., WECKER, E. & GARD, S. **Genetic Markers and Serological Identity of Wild and Attenuated Strains of Type 1 Poliovirus, with special emphasis on Strains isolated from Patients during an Epidemic in the Belgian Congo.** *Bull. World Health Organization*. Geneva. 1960, v. 22, Nos. 3/4, 243–53. [14 refs.]

The occurrence of an epidemic of type 1 poliovirus in Léopoldville about 2 months after the initiation of a mass vaccination programme with the attenuated CHAT strain [see p. 794] made it imperative to assess whether there had been a change in virulence of the CHAT strain responsible for the outbreak. An analysis was made of several characters of viruses isolated from non-vaccinated patients suffering from paralytic poliomyelitis in Léopoldville, from persons fed CHAT virus in Léopoldville and from 12 patients fed the CHAT strain in the U.S.A., 2 of whom had acquired infection by contact, 1 as a second member of a chain of infection and the other as a third member. 4 characters of these viruses and also a naturally attenuated and virulent strain of type 1 poliovirus were examined for (1) antigenic structure by counting the proportion of plaques produced under agar containing anti-CHAT serum, (2) the d character, d+ virus being able to grow under agar containing low amounts of sodium bicarbonate [this *Bulletin*, 1958, v. 33, 801], (3) ability to grow in MS cells [KANDA and MELNICK, *ibid.*, 1959, v. 34, 586]. MS+ strains are able to grow equally well in the stable line of monkey kidney cells as they are on fresh monkey kidney cells. (4) Growth at 37° and 40°C. t+ strains are able to grow equally well at 40° as at 37°C. t− strains, on the other hand, have a titre 10^4 to 10^5 lower at 40° than at 37°C. The results confirm previous observations that virulent strains show the characters d+, MS+, t+, exemplified by the Mahoney strain, and that attenuated strains, like CHAT, are d−, MS− and t−. It was also found that the CHAT strain and the Mahoney strain differed in serological characters. It was found that the strains isolated from patients in Léopoldville were in general different serologically from CHAT, were d+, MS+ and t+ or showed intermediate reactions, whereas the strains isolated from persons fed the CHAT virus even after 2 or 3 passages resembled the CHAT strain in character. Although noting that t study was carried out on rather few strains of poliov the authors conclude that the virus isolated from para patients in Léopoldville was not related to the CH strain. They also note that the excreted CHAT str studied showed a high degree of genetic stability, recognize that more strains have to be examined be establishing this point beyond question. The aut admit that it is possible that the epidemic strain derived from the CHAT strain by mutation, but p out that there is no evidence from their labora studies in favour of this view. *A. J. Bea*

KOCH, G., KOENIG, Susan & ALEXANDER, Hattie **Quantitative Studies on the Infectivity of R nucleic Acid from Partially Purified and Hig Purified Poliovirus Preparations.** *Virol.* New York. 1960, Mar., v. 10, No. 3, 329–43, 3 [16 refs.]

RNA obtained by phenol extraction from poliov will infect susceptible cells [also some cells not sus tible to intact virus, see DE SOMER *et al.*, this *Bull* 1960, v. 35, 204] but the degree of infectivity is much less than that of the intact virus from which RNA was derived. Infectivity of RNA depends upon titre of intact virus (*i.e.*, does not require some cell c ponent in addition). The recovery of RNA is impro if the phenol does not contain hypophosphorous sometimes used as a preservative. The efficiency phenol extraction did not differ in the range 0°–5C but the *p*H during extraction must be held between 7·4. The recovery of infectivity of RNA was most de dent on the molarity and *p*H of the medium use dilute the RNA when placed in contact with cells. molarity and *p*H should be as high as the cells stand. Similarly, prewashing cells with 0·6 M soc chloride increased the infectivity of an RNA prepara 5-fold. Cells differ in their ability to withstand hypert solutions but a strain of human amnion cells (FERNAN *Texas Rep. Biol. & Med.*, 1958, v. 16, 48) can w stand 1·5 M KCl whereas most cells cannot withs 1·2 M or more. Similarly, the highest *p*H that car used is 8·2. Since storing the RNA in isotonic solu does not affect the infectivity provided exposure to is in hypertonic solution, and since the number plaques produced is a linear function of RNA dilutio seems that prevention of disaggregation is not the rol hypertonic solutions in preserving infectivity. By ana with the findings of the increased rate of pinocytosi amoebae in strong salt solutions (CHAPMAN-ANDRE *C. R. Trav. Lab. Carlsberg, Sér. Chim.*, 1958, v. 31, 7 is suggested that the effects of *p*H and hypertonic s tions may be to make cell membrane more pervious receptive to RNA.

[See also this *Bulletin*, 1959, v. 34, 177.] *A. J. Bea*

POLSON, A., EHRENBERG, A. & CRAMER, R. **Investi tions of Poliomyelitis Antigens.** *Biochim. Biophys. Acta.* 1958, Sept., v. 29, No. 3, 612 13 figs. [14 refs.]

" Preparations of types I and II of polio virus been found by sedimentation analysis to contain t

tinct components with sedimentation coefficients of 6 *S*, 70–95 *S* and 15–25 *S* respectively. The Stockholm strain of Type I virus has a greater ratio of more owly to more rapidly sedimenting material than the ner preparations investigated. A diffusion coefficient 1·5 F has been estimated for the 156 *S* component. fectivity tests following separation centrifugation of one mple indicate that the two faster components are both fective. The Type III virus appeared homogeneous in ultracentrifuge."

OLSON, A., EHRENBERG, A. & CRAMER, R. **Specific Precipitin Reactions of the Virus of Poliomyelitis in Gels.** *Biochim. et Biophys. Acta.* 1958, Sept., v. 29, No. 3, 622–9, 10 figs. [16 refs.]

"By means of precipitin tests, preparations of Type I olio virus have been found to contain at least three antinically active components. The three precipitin bands ve tentatively been correlated to the three distinct comnents observed in the ultracentrifuge. Type II also ntains more than one antigen but the secondary bands e weaker. A lyophilized sample produced a precipitin ttern very similar to that formed by the untreated virus, spite of the drastic changes in virus infectivity and rticle size following this treatment. The Type III virus peared to be antigenically homogeneous. No cross retions could be observed between the different virus pes and immune sera."

ARD, S. **Immunological Strain Specificity within Type 1 Poliovirus.** *Bull. World Health Organization.* Geneva. 1960, v. 22, Nos. 3/4, 235–42. [10 refs.]

At the present time there is an extensive search for an dequate genetic marker to characterize strains of attenued poliovirus so that they can be tagged during their pread in a vaccinated community. The discovery of ICBRIDE [this *Bulletin*, 1959, v. 34, 833] and WENNER *et l.* [*ibid.*, 1301] that antigenic differences between strains f 1 type of poliovirus can be recognized has stimulated he investigation of antigenic markers for this purpose. n this paper Gard describes a simple modification of his mmuno-inactivation technique [*ibid.*, 1958, v. 33, 288] hich enables a rapid antigenic screening of strains to be arried out. It was found that the specificity of sera btained from individual animals showed marked variaons and the importance of selecting a good animal ather than using sera pooled from several animals for his sort of investigation is pointed out. A variety of trains of type 1 poliovirus isolated in the epidemic preiously described in Léopoldville [pp. 794, 822] and rom individuals fed the CHAT strain either in the J.S.A. or in Sweden were examined with the use of an nti-serum prepared against the CHAT strain and also one prepared against a virus, Likubukide No. 81, isolated rom a patient with paralytic poliomyelitis in Léopoldville. These 2 viruses were shown to be antigenically ifferent. It was found that most of the strains isolated rom Léopoldville were similar to Liku as was the Mahoney strain. 11 strains isolated from people fed the CHAT virus in the U.S.A. were similar to CHAT and different from Liku. However, 2 out of 5 strains isolated from persons fed CHAT virus in Sweden showed differences from the CHAT strain in this test. The author is cautious in drawing conclusions from his experiments but believes that his technique offers a simple and reliable method of screening strains for antigenic characters. In addition, he believes that it is possible for minor antigenic changes to occur during the passage of CHAT virus through the human intestinal canal although such changes are presumably not common. *A. J. Beale*

HAAS, R., THOMSSEN, R., DOSTAL, V. & RUSCHMANN, E. Untersuchungen zum Mechanismus der Formaldehydinaktivierung von Poliomyelitisviren. [**Investigations on the Mechanism of Action of the Inactivation of Poliomyelitis Virus by Formaldehyde**] *Arch. f.d. gesamte Virusforschung.* 1959, v. 9, No. 4, 470–83, 7 figs. [23 refs.]

An investigation has been made of the effect of amino-acids and of dialysis upon the rate of inactivation of the Mahoney strain of type 1 poliomyelitis virus by formaldehyde. Inactivation was carried out with volumes of 500 cc. at 37°C. with the addition of formaldehyde in a concentration of 70 μgm. per cc., and the course of the process was followed by the titration of 10 cc. samples removed at intervals. The rate of inactivation could be increased by decreasing the amount of nitrogen in the medium by diluting it with Hanks solution; the nitrogen content was linearly related to the inactivation rate, and also to the residual concentrations of formaldehyde present after 24 hours. The inactivation was markedly inhibited by the addition of cysteine, histidine or sodium bisulphite in the proportion of 5 molecules to 1 molecule of formaldehyde. A slight increase in titre was observed immediately after the addition of histidine, possibly due to the recovery of a small proportion of inactivated particles. In plaque titrations carried out on dialysed samples the rate of formation of plaques became slower as the inactivation proceeded, but the rate could be restored by the addition of histidine, and regained the normal value in virus which had been inactivated with formaldehyde for 15 hours and then exposed to the action of histidine for 5 days. The rate of plaque formation could also be restored to normal by dialysing the inactivated virus against Hanks solution at 25°C., but dialysis at 4°C. was ineffective, even in the presence of histidine.

The results thus indicate that the inactivation of the virus by formaldehyde is partly reversible, and that in tests of inactivation of batches of vaccine dialysis should be carried out at 25°C. and not in the cold.

D. J. Bauer

NORMAN, A. **Ultraviolet Inactivation of Poliovirus Ribonucleic Acid.** [Correspondence.] *Virology.* New York. 1960, Mar., v. 10, No. 3, 384–7, 1 fig. [13 refs.]

Poliovirus and tobacco mosaic viruses (TMV) contain RNA of similar molecular weight yet poliovirus is 18 times more sensitive than TMV to ultraviolet light.

Comparison of the UV inactivation of poliovirus RNA with published figures of SIEGEL *et al.* (*Nature*, 1956, v. 178, 1117) for TMV RNA reduces this discrepancy to 30%. Whereas TMV RNA is more sensitive than intact virus, poliovirus appears to be about twice as sensitive to UVL as the RNA extracted from it. *A. J. Beale*

FURESZ, J. **The Antibody Response of Roosters to Poliomyelitis Virus.** *J. Immunology.* 1960, Mar., v. 84, No. 3, 251–7, 1 fig. [27 refs.]

6–12 month old roosters showed a good antibody response to either living or formaldehyde-inactivated poliovirus. A combined intravenous and intramuscular inoculation gave the highest titres, and the intravenous route better responses than the intramuscular. 3 inoculations were given, the first 2 at 7 days' interval and the third 4 weeks after the second. With single types of living virus it was found that high titres of antibody were obtained against the inoculated type. However, heterotypic responses also occurred especially with type 2 virus where both type 1 and 3 antibodies were produced. Type 1 virus elicited type 2 antibodies also but not type 3. Type 3 only elicited occasional very low titre type 2 and more rarely still type 1 antibodies in addition to the specific antibodies. It was found that 1 dose in roosters intravenously gave very similar titres to those in monkeys after 3 doses of poliovaccine inactivated with formalin and much higher titres after 2 or 3 doses. It is suggested that roosters could be used with advantage for potency tests of killed poliovaccine. *A. J. Beale*

LÉPINE, P., ROGER, F., SAUTTER, V. & ROGER, A. La réaction cinétique de séro-neutralisation des virus poliomyélitiques en culture cellulaire. 2. Application à l'étude de l'antigénicité des vaccins antipoliomyélitiques sur poussins (méthode de l'Institut Pasteur). [**The Kinetic Reaction for Measuring Serum Neutralizing Antibody against Poliovirus. 2. Application to the Study of the Antigenicity of Polio Vaccines in Chicks (Pasteur Institute Method)**] *Bull. World Health Organization.* Geneva. 1960, v. 22, Nos. 3/4, 273–89, 6 graphs.

This paper gives very complete details of an accurate method of potency determination for monovalent or trivalent poliovaccines. Groups of 12 7-day-old chicks (New Hampshires) were inoculated with 1 ml. of vaccine undiluted, and diluted 1/10 and 1/100. 14 days later a second dose was given and 7 days later the animals were bled. A mixture of the 3 types of living virus was used as a standard preparation. The individual sera were titrated by the kinetic method in KB cells previously described [LEPINE *et al.*, this *Bulletin*, 1960, v. 35, 93]. After probit transformation the plot of log concentration of vaccine against per cent. of animals with antibodies is a straight line. From this line the dose giving a 50% response can be read off. This is an accurate measure of vaccine potency. This method is applicable not only to inactivated virus but also to living and partially inactivated virus. *A. J. Beale*

TOBIN, J. O'H. **Notes on Viruses likely to be countered in Vaccine Production using Mon Kidney Material.** *Bull. World Health Organ tion.* Geneva. 1960, v. 22, Nos. 3/4, 431–3. [R in footnotes.]

This is a short but remarkably complete accoun the viruses carried by monkeys which may be encount when monkey tissues are used for preparing vaccine. hazard of contamination by these viruses has been de mined mainly during the production of killed polio cine, but assumes even greater importance when li poliovaccines are contemplated. Since the viruses sp from monkey to monkey they can be controlled to a g extent by quarantining the animals. The main group viruses are: Virus B; Simian viruses, some of which duce cytopathic changes and some haemadsorpt measles-like virus and foamy agent. Foamy appear in monkey kidney cells is very frequent but only a portion of cultures showing these changes are infe with a transmissible agent. Arbor viruses and pox vir have also been isolated. *A. J. Bea*

KRECH, U. **The Determination of Antigenic Pote of Poliomyelitis Vaccine by Measuring its A body-Combining Capacity.** *Bull. World He Organization.* Geneva. 1960, v. 22, Nos. 3/4, 3 11. [11 refs.]

A method of determining the antigenic potency poliovaccines by means of an antibody combining pc test is described in detail. In principle the test invo mixing vaccine dilutions with antiserum capable of re ing the titre of poliovirus about 95%. After a perio reaction a standard dose of virus is then reacted with immune serum and the immune serum pretreated vaccine. A standard vaccine is put up with each b of test vaccines and their potency expressed as a rati the standard. *A. J. Bea*

HAAS, R., DOSTAL, V. & THOMSSEN, R. Ein Beitrag Frage der zeitlichen Gliederung der staatlic Wirksamkeitsprüfung der Poliomyelitisimpfst [**A Contribution to the Question of the Timin the Official Potency Testing of Poliomye Vaccines**] *Ztschr. f. Hyg. u. Infektionskr.* 1 v. 146, No. 1, 8–12.

The authors have investigated the duration of pe tence of neutralizing antibody to the 3 types of p myelitis virus in guineapigs inoculated with vaccine taining 0·7 mgm. per cc. of Al_2O_3 in accordance the legal requirements of the German Federal Repu for the testing of poliomyelitis vaccines. 5 batche vaccine were each tested in groups of 12 guinea which were given 3 doses of 2 cc. of vaccine su taneously with intervals of 7 days. Blood samples fo neutralization tests were taken from 3 animals at statutory time of 14 days after the last injection, and from the remaining animals in groups of 3 after 3 and 74 days. The neutralization titres obtained wer the expected order, and showed no essential decline

period of observation. It is therefore concluded the time after which the neutralization test is carried could be considerably prolonged without affecting the ssment of the potency as far as vaccines containing stated amount of adsorbent are concerned.

D. J. Bauer

MÖK, I. **Studies on the Interaction between Coxsackie and Poliomyelitis Viruses. IV. Further Experiments concerning the Antagonism between Coxsackie B1 Virus and the Lansing Strain of Policmyelitis Virus in Young Mice.** *Acta Microbiologica.* Budapest. 1960, v. 7, No. 1, 87–93. 1 fig. [13 refs.]

n a series of interesting papers the author has shown 9-day-old mice surviving infection with Coxsackie B1 us are resistant to super-infection with mouse-adapted iovirus (Lansing strain of type 2) for at least 60 days. has now shown that previous Coxsackie B1 virus ction inhibits poliovirus multiplication in the CNS. o Coxsackie B1 virus persists as a chronic infection in e infected at 9 days for at least 18 days and probably ch longer. Using special methods to remove Coxsackie antibody Coxsackie B1 was isolated from mixed liver pancreas suspension of 2 mice infected 43 days previly. It is suggested that persistence of Coxsackie B1 us despite the presence of specific antibody causes the rference with poliovirus growth. *A. J. Beale*

M, K. A. & BENYESH-MELNICK, Matilda. **Typing of Viruses by Combinations of Antiserum Pools. Application to typing of Enteroviruses (Coxsackie and ECHO).** *J. Immunology.* 1960, Mar., v. 84, No. 3, 309–17, 3 figs.

A large number of enteroviruses have now been identi- (3 polioviruses, 6 Coxsackie B, 28 ECHO and over Coxsackie A) so that the problem of their identifica- becomes formidable. The usual practice is to use ols of antisera as a screening procedure and then to ak down the pools by testing against each individual e in the mixture neutralizing the virus. Thus all polio- uses will be neutralized by a mixture of the 3 antisera l the type identified by tests with the individual sera. e authors describe an ingenious series of combinations antisera such that from the pattern of neutralization the pools a virus isolate can be identified in one step. us, for example, with 7 pools each containing 10 sera unique patterns of neutralization can be achieved by ng suitable mixtures of antisera. The feasibility of s scheme depends upon having potent monospecific tisera and keeping the possibility of mixtures in mind. e practical application of a system using 7 pools, 4 ntaining 7 sera and 3, 8 sera, is presented. In this heme no virus was recognized by neutralization by only ool, *i.e.* antisera to each of the 24 viruses appeared in least 2 combinations. Thus a virus mixture would mediately declare itself by being neutralized by only 1 mbination (*i.e.* the one that had antibodies to both ruses) or by not being neutralized at all. A few mixes could still cause confusion but inspection of the antisera combinations would readily reveal these. The scheme for enteroviruses other than poliovirus proved to be practical in the investigation of unknown viruses provided that viruses that had grown through mixed poliovirus antisera were tested.

[This interesting paper should be read in the original by any laboratory contemplating setting up this identification scheme.] *A. J. Beale*

ANDRÉ, J. & AUDEBAUD, G. Recherches sur les virus entériques de *Macacus cynomolgus.* [**Studies on Enteric Viruses in Cynomolgus Monkeys**] *Bull. Soc. Path. Exot.* 1959, Nov.–Dec., v. 52, No. 6, 751–8.

The results of a study of the viral flora of the faeces of cynomolgus monkeys in Saigon are described. On the basis of the appearance of cytopathic effects 2 groups of viruses were distinguished, those like adenoviruses and those like polioviruses. 2 successive rectal swabs, with an interval of 3 days between them, from 18 monkeys were examined in monkey kidney tissue culture. Each swab was tested on 2 separate occasions. All the animals except 4 were excreting a virus and several of the animals excreted both adeno- and polio-like viruses.

A. J. Beale

FELICI, A.; GORI, G. B.; MANCINI, G.; CASTELLI, L.; BALDUCCI, D. Contributo allo studio dei virus della scimmia. I. Virus citopatogeni isolati dai reni e dalle feci di scimmie asiatiche ed africane [**A Contribution to the Study of Simian Viruses. I. Cytopathic viruses isolated from the Kidneys and Faeces of Asiatic and African Monkeys**] [FELICI, GORI, MANCINI & CASTELLI] *Riv. Istituto Sieroterap. Ital.* 1959, July–Aug., v. 34, No. 4, 299–303. English summary (9 lines). II. Isolamento di un virus latente dal midollo spinale di una scimmia sana [**II. Isolation of a Latent Virus from the Spinal Cord of a Healthy Monkey**] [MANCINI, CASTELLI, BALDUCCI & FELICI]. *Ibid.*, 304–6. English summary.

The authors have isolated 51 strains of virus from rectal swabs taken from 85 rhesus monkeys. On the basis of their cytopathic effects 17 of these strains were considered to be adenoviruses and 33 to be enteroviruses. 5 strains of virus which were isolated from cultures of apparently normal monkey kidney cells produced a cytopathic effect resembling that of poliomyelitis virus. Another strain was isolated in monkey kidney cell cultures from the cervical region of the spinal cord of an apparently healthy rhesus monkey which had been used for the safety testing of poliomyelitis vaccine. A cytopathic effect was produced which at first resembled that of poliomyelitis virus, but after the affected cells had come off the glass one culture recovered; the same phenomenon was seen in 3 successive passages, but on the 4th passage the effect progressed to complete destruction of the culture. The virus would not multiply in human kidney, HeLa, KB or monkey heart cells, and was not pathogenic for laboratory animals. It was not neutralized by antisera to B virus and 11 simian viruses.

D. J. Bauer

BENSON, Lois M. & HOTCHIN, J. E. **Cytopathogenicity and Plaque Formation with Lymphocytic Choriomeningitis Virus.** *Proc. Soc. Exper. Biol. & Med.* 1960, Mar., v. 103, No. 3, 623–5, 1 fig.

Cytopathic effects and plaques under agar were produced in trypsinized chick embryo cells by LCM virus either direct from mouse brain suspensions or after serial passage in tissue culture. This is the first observation of cytopathic effects with this virus. Apparently, although the virus multiplied reaching maximal titres by 7 days, cytopathic effects and plaque formation were not produced for about 12 days. Plaques formed rapidly over the 11th night as a rule. The main difficulty experienced with the plaque assay was preserving healthy cells under agar for 12 days. The sensitivity of the assay systems were very close but in order of sensitivity were LD50 in mice, TCD50 determined by cytopathic effects in tubes, and plaque-forming units. *A. J. Beale*

SCHEID, W., ACKERMANN, R., JOCHHEIM, K. A. & LEHMANN-GRUBE, F., with the technical assistance of G. LIEDTKE & H. FUCHS. Die neutralisierenden Serumantikörper des Menschen nach Infektionen mit dem Virus der lymphozytären Choriomeningitis und das Verhalten von Normalseren im Neutralisationsversuch. [**Neutralizing Antibodies in Man after Infection with Lymphocytic Choriomeningitis Virus and the Behaviour of Normal Sera in the Neutralization Test**] *Arch. f.d. gesamte Virusforschung.* 1959, v. 9, No. 3, 295–309, 1 fig. [Numerous refs.]

By means of intracerebral neutralization tests carried out in mice it was found that freeze-drying had little effect upon the titre of neutralizing antibody to lymphocytic choriomeningitis virus in human immune sera, which retained their titre when stored for several years. Liquid sera stored at temperatures ranging from −20° to −30°C. showed a loss of titre of around 0·5 log unit after 14 days, and a loss of 1 log unit was observed at 4°C. or room temperature. Heating at 56°C. for 30 minutes caused a loss of titre of 2 log units. Neutralization of virus to an extent ranging from 0·6 to 1·85 log unit was constantly found in the examination of the sera of 36 persons aged from 18 to 64 years who had never undergone any recognizable infection with lymphocytic choriomeningitis virus. The sera of 15 persons who had suffered from confirmed lymphocytic choriomeningitis had an average neutralization index of 4·5 log units. In a number of cases it was possible to follow the antibody titre over an extended period; the maximum values (around 4–5 log units) were attained after 68–126 days, and in 3 cases titres of the same order were still found 358, 762 and 1439 days after infection. *D. J. Bauer*

LEHMANN-GRUBE, F. Untersuchungen zur Wärmestabilität des Virus der lymphozytären Choriomeningitis. [**Investigations on the Heat Stability of Lymphocytic Choriomeningitis Virus**] *Arch. f.d. gesamte Virusforschung.* 1959, v. 9, No. 1, 56–63.

In an investigation of the thermal inactivatio lymphocytic choriomeningitis virus carried out by r ted intracerebral titrations in mice no loss of titre be detected in a suspension of infected mouse bra saline or 10% rabbit serum during storage for 336 at −70°C. A suspension of mouse brain in saline an initial titre of 5·12 log units had declined in tit 0·4 log unit after storage at 2°C. for 20 hours and could no longer be found after 168 hours, where suspension in 10% rabbit serum retained its titre this period. The effect of various diluents was investigated, and saline was found to give lower than 10% rabbit serum or phosphate buffer. *D. J. Ba*

LEHMANN-GRUBE, F., ACKERMANN, R., JOCHHEIM, K LIEDTKE, G. & SCHEID, W. Über die Technik Neutralisation des Virus der lymphozytären Ch meningitis in der Maus. [**The Techniqu Neutralization of Lymphocytic Choriomenin Virus in the Mouse**] *Arch. f.d. gesamte V forschung.* 1959, v. 9, No. 1, 64–72, 1 fig. [Nu ous refs.]

The authors have investigated the influence of va factors upon the results of neutralization tests lymphocytic choriomeningitis virus. The tests were ried out by adding a constant volume of immune s to several decimal dilutions of the virus preparation mixtures were incubated at 37°C. for 2 hours and injected intracerebrally into groups of 6 mice. Som lower neutralization titres were found when older were used, and in further experiments in which 4 g of 50 mice of different ages were used it was found 28 gm. mice gave a neutralization titre of 4·6 log compared with 5·35, 6·25 and 5·89 log units for weighing 23, 16 and 14 gm. respectively. No neutr tion could be obtained when the incubation was c out at 2°C. Considerable loss of specific neutra power was observed when the immune serum was h at 56°C. for various periods up to 60 minutes. In tralization tests carried out with a range of dilutio immune serum the neutralization index showed a regression on log serum dilution with a regre coefficient of −3·2. *D. J. Ba*

LIBÍKOVÁ, H. **The Problem of the Transmis Encephalitis in the Light of the Natural F Theory.** *J. Hyg., Epidemiol., Microbiol. & munol.* Prague. 1960, v. 4, No. 1, 66–80. [Nu ous refs.]

This is a review of what is known about the ma ance in nature of arborviruses. Tick-borne and mos borne encephalitis viruses are reviewed in turn. changing and evolving nature of natural foci of infections is stressed, and the study of such foci de on team-work between virologists, parasitologist zoologists. *C. E. Gordon Sm*

ÁCEK, J. **Experimental Hibernation of the Virus of the Eastern Type of North American Equine Encephalomyelitis (EEE) in Czechoslovak Species of Ticks (*Ixodes ricinus* L. and *Dermacentor marginatus* Sulz).** *J. Hyg., Epidemiol., Microbiol. & Immunol.* Prague. 1960, v. 4, No. 1, 61–5, 1 fig. [26 refs.]

he Cg strain of eastern equine virus after 25 mouse sages was used. All developmental stages of tick e infected by feeding on infected young mice, adult ales being allowed to feed serially on new infected e as the latter died in 2–3 days. The engorged ticks e placed in an iron cylinder packed loosely with grass leaves, which was then buried to its upper rim in the ural habitat of *Ixodes ricinus*. They were infected buried in December and the ticks were examined for is in February. None of the ticks died and virus was nd in larvae and nymphs of *I. ricinus* after 86 days' ernation and in adult females after 66 days' hiberna- n although the titre of virus in them had fallen. Virus s not demonstrated in females of *Dermacentor margin- s* or in males of either species. A guineapig on which half-engorged *D. marginatus* were fed showed no evi- ce of infection and did not form antibodies. Virus s not found in eggs or larvae from the *I. ricinus* or m the females after they had laid the eggs.

C. E. Gordon Smith

TRICK, F. M., YANCEY, Frances S., HANSEN, P. A. & BYRNE, R. J. **Hemagglutination-Inhibition and Serum Neutralization Response of Horses to Eastern Equine Encephalomyelitis Virus.** *Proc. Soc. Exper. Biol. & Med.* 1960, Mar., v. 103, No. 3, 549–51. [13 refs.]

The V-52 strain of eastern equine virus isolated from naturally infected horse and after 17 mouse passages s used. 3 horses from non-enzootic areas were inocu- ed intradermally and 1 subcutaneously with about 10^6 ouse LD50. Serum was collected at intervals. Intra- ebral virus-dilution neutralization tests in mice were ed. The haemagglutinin-inhibition (HI) tests were ne on acetone-extracted sera with a centrifuged-alka- e-extract antigen. None of the horses had antibody fore infection. All 4 had HI antibody 5 days after oculation and the maximum titre (320–1280) was ached after 10–14 days falling to 20–160 after 9–12 onths. The neutralizing indices reached 50 10–14 days ter inoculation and remained above 100 up to 12 onths. None of the horses had symptoms.

73 sera from horses and ponies from areas of Maryland d Virginia where eastern equine encephalomyelitis had curred at least 8 months previously were tested. 59 d neither neutralizing nor HI antibody. The remainder d neutralizing indices from 2·0–2·9 log. 9 of the also had HI antibody titring 10–320 against 2 its of antigen, 6 [? of 13] had antibody against 4 units, d 5 [? of 13] against 8 units. *C. E. Gordon Smith*

AITKEN, T. H. G., DOWNS, W. G., ANDERSON, C. R., SPENCE, L. & CASALS, J. **Mayaro Virus isolated from a Trinidadian Mosquito, *Mansonia venezuelensis*.** *Science.* 1960, Apr. 1, v. 131, 986.

11% of 615 Trinidad people had Mayaro neutralizing antibody and rates as high as 48% were found in the south-east [this *Bulletin*, 1959, v. 34, 611]. The virus was isolated in 1954 from a forest worker in this area and from 5 other persons during August–September [*ibid.*, 1958, v. 33, 536]. It was not encountered again until it came in March 1957 from a pool of 49 *Mansonia venezuelensis* which were taken coming to bite man in the Rio Grande Forest in north-east Trinidad. The virus was isolated and re-isolated in baby mice and also in hamster kidney cultures. By complement-fixation, haemagglutinin-inhibition and neutralization tests it was indistinguishable from Mayaro virus. The new isolate is pathogenic intracerebrally to adult mice which the original isolate was not; it also multiplies in chick embryo cultures without cytopathic effect unlike the original strain. This is the first isolation of Mayaro virus from wild-caught arthropods. *C. E. Gordon Smith*

FAN, Tszi-Min. **Cultivation of Japanese B and West Nile Encephalitis Viruses in Tissue Cultures.** *Problems of Virology.* London. 1959, v. 4, No. 2, 82–7, 2 figs. [10 refs.] [Translated from Russian.]

5 strains of Japanese encephalitis (JE) and 1 of West Nile (WN) virus were used, as were SOTs (derived from cynomolgus monkey heart) and HeLa cells, and plasma-clot preparations of skin muscle from human and chick embryos. 5–12 passages were made in SOTs cells with 3 strains of JE and the WN, log titres of about 6·0 being maintained. Cytopathic changes were found from the 1st passage starting in 3–4 days. 1 strain of JE grew but failed to cause cytopathic effect. 8–12 passages were made in HeLa cells, 1 strain of JE and the WN caused cytopathic effects but 1 other strain of JE did not and a further strain only at the 11-12 passage level and not in later passages. 5–18 passages were made in human embryo skin-muscle—titres averaged 5·6 log but no marked cytopathic effects were seen. 6–8 passages were made in chick embryo skin-muscle with an average titre of 5·0 log but no cytopathic effects were seen. The cytopathic changes in SOTs and HeLa cells were confirmed in neutralization tests. *C. E. Gordon Smith*

RADVAN, R., HANZÁK, J., HEJNÝ, S., REHN, F. & ROSICKÝ, B. **Demonstration of Elementary Foci of Tick-Borne Infections on the Basis of Microbiological, Parasitological and Biocenological Investigations.** *J. Hyg., Epidemiol., Microbiol. & Immunol.* Prague. 1960, v. 4, No. 1, 81–93, 9 figs.

Within the endemic areas, Q fever and tick-borne encephalitis virus seem to occur in numerous very small foci. 2 such foci were studied in a foothills area 300–500 m. above sea level with a rainfall of 700–800 mm. per annum. One-third was unbroken forest (mainly coniferous) and the rest fields mainly around agricultural

villages. Ticks commonly bite man in this area but goats do not enter the forested areas.

The first focus studied was in a young fir forest with patches of marsh forest in the centre. The second was a marshy hollow of mixed trees and vegetation surrounded by fir plantations. Throughout a year ticks were collected by dragging along two 2m. strips diagonally across the foci—numerous *Ixodes ricinus* were obtained in both. 1 strain of *Coxiella* [*Rickettsia*] *burneti* and 1 of tick-borne encephalitis virus were isolated from *I. ricinus* in the first focus and 1 strain and 3 respectively in the second focus where *C. burneti* was also isolated from a shrew (*Sorex araneus*). Tick-borne encephalitis antibodies were found in a deer in each and in a rabbit in the second. The fauna and flora of the foci are described in detail. Such foci depend on the concurrence of suitable conditions (microclimate, shelter, food, etc.) for the maintenance of the ticks and their vertebrate hosts.

C. E. Gordon Smith

GRESÍKOVÁ, M. & ŘEHÁCEK, J. Isolierung des Zeckenenzephalitisvirus aus Blut und Milch von Haustieren (Schaf und Kuh) nach Infektion durch Zecken der Gattung *Ixodes ricinus* L. [**The Isolation of Tick-borne Encephalitis Virus from the Blood and Milk of Domestic Animals (Sheep and Cows) after Infection by Ticks of the Species** *Ixodes ricinus* **L.**] *Arch. f.d. gesamte Virusforschung.* 1959, v. 9, No. 3, 360–64. [10 refs.]

Ticks of the species *Ixodes ricinus* were allowed to feed on mice infected with a mouse-adapted strain of louping-ill virus which was no longer pathogenic for lambs. After 2–3 days the ticks were removed, and titrations carried out with a suspension of some of them showed that they contained virus in a titre of 10^4–10^5. The remaining ticks were allowed to bite 2 ewes, 30 being attached to each animal. Apart from a transient rise of temperature no signs of illness were observed, and no viraemia, although neutralizing antibody was found in titres of 800–1000 3 months later. Louping-ill virus could be isolated from the milk of one of the animals. In similar experiments with tick-borne encephalitis virus carried out on 2 ewes no signs of illness could be observed, but the virus could be isolated from the blood and the milk of both animals 3–7 days after infection, and neutralizing antibody could be found after 2 weeks. A cow infected in a similar manner with tick-borne encephalitis virus showed no signs of illness, but the virus could be isolated from the blood on the 2nd and 6th days and from the milk on the 3rd and 4th days after infection. The implications of these results for the epidemiology of the 2 diseases is pointed out.

D. J. Bauer

ZASUKHINA, G. D. **Studies of the Development of Tick-Borne Encephalitis Virus in Cultures of Human and Animal Tissues.** *Problems of Virology.* London. 1959, v. 4, No. 2, 71–7. [Translated from Russian.]

The Sof'in strain of RSS virus in high mouse-passage was used. Plasma clot cultures of skin-muscle, lung and kidney from human embryos, of skin-muscle from and rats, and of chick embryo tissues were used, as trypsinized monkey and dog kidney cells and HeLa 40 passages were successfully made in human em skin-muscle, 5–7 passages in human embryo, kidney lung, in HeLa cells, in mouse, rat and chick embryo sues, and 4 passages in monkey and dog kidney Maximum virus titres were reached after 3–8 days decreased thereafter. Highest titres (6·3–6·5 log L were obtained in human embryo skin-muscle and H cells. In the former, virus could be detected 44 after infection in cultures in which the medium had been changed. Marked cytopathic effect was seen human embryo skin-muscle from the 1st passage and titres in tissue culture were similar to those by mi titration. The cytopathic effect was lost if the inocu was stored frozen between passages although the itself survived [but ? at a lower titre]. The cytop effect was neutralized by specific antiserum. HeLa had virus titres as high as human embryo skin-muscle did not show cytopathic effects, perhaps because t effects are confined to cells of connective tissue orig embryo rat skin-muscle also showed cytopathic eff The presence of salts, and horse serum rather than bo serum, enhanced the cytopathic effects.

C. E. Gordon Smi

KARPOVICH, L. G. & ZASUKHINA, G. D. **Cultiva of Viruses of the Tick-Borne Encephalitis Gr in SOTs Cells.** *Problems of Virology.* Lon 1959, v. 4, No. 2, 88–92, 3 figs. [Translated fr Russian.]

5 strains of tick-borne encephalitis, 3 of biphasic m ingo-encephalitis and 2 of louping-ill virus were used.. multiplied readily in 5–8 passages in SOTs cells. maximum titres were reached 2–6 days after inocula Marked cytopathic changes (less marked in early pas in 2 strains) were seen from the 1st passage; these b after 24 hours and were complete by the 5th day. I ula could be stored for 2 days at −20°C. without los ability to cause cytopathic changes. The specificit these changes was demonstrated by neutralization t Tissue culture fluids titrated in parallel in mice and ti cultures gave titres differing by only 0·5–1·0 Mouse brain titrated in the 2 systems gave higher t (1·5–2·0 log) in mice.

C. E. Gordon Smi

GRESÍKOVÁ-KOHÚTOVÁ, M. **The Effect of Heat Infectivity of the Tick-Borne Encephalitis Vi** *Acta Virologica.* Prague. 1959, Oct., v. 3, No 215–21, 4 figs.

The Hypr strain of virus after 40 mouse passages used. Mouse-brain suspensions in buffered saline 7·4), milk and other fluids were heated in sealed ampo then cooled and titrated by intraperitoneal inoculatio mice. Heating at various temperatures for 20 minu 50° but not 45°C. destroyed virus in saline and 65° 70°C. was needed to destroy the same amount of viru milk. In saline 55°C. for 15 minutes killed the vi when 10% of rabbit serum was added 55–60°C. fo

utes inactivated it, but in milk 65°C. for 15 minutes required. Heated in saline for 20 minutes the titre pped 1·2 log at 40°C., 2·1 log at 45°C., 2·7 log at C., >3·7 log at 55°C.; in saline with 10% rabbit m there was no loss of infectivity at 40–45°C., but e was 5 log loss at 55°C. and >6 log at 62°C.: in no loss occurred at 40–45°C. and only 1 log at 50–C.; after 20 minutes at 65°C. however, virus could not detected at 10^{-2}. At 62°C., the pasteurization tem-ature in the "holding" method, virus was not com-ely inactivated. Boiling for 1 minute destroyed the s. As infections with this virus occur by ingestion infected milk and milk products, these studies are portant. *C. E. Gordon Smith*

LKOVÁ, D. & FRAŇKOVÁ, V. **The Lymphatic System in the Development of Experimental Tick-Borne Encephalitis in Mice.** *Acta Virologica.* Prague. 1959, Oct., v. 3, No. 4, 210–14, 2 figs. on 2 pls. & 1 text fig.

he Hypr strain of virus in its 39th mouse passage was d. The lymphatic system of the mice was defined by ction of Indian ink. When 10^6 LD50 of virus was cted into a hind paw, virus was detected in the pop-al nodes after 30 minutes, also in the upper para-tic nodes after 75 minutes and in the blood only after minutes. The regional nodes were removed from a e limb and 10^4 LD50 then inoculated into the corres-ding paw. After 12 hours slight viraemia was present a control mouse but undetectable in the mouse with-nodes in which viraemia was detected only after 48 rs. In mice infected in the fore limb the lymph node the infected limb contained 10^3–10^4 LD50 of virus m 24 hours after infection, and similar titres were nd in the nodes of the hind limb from about 12 hours r; the blood titred about $10^{1·5}$ LD50 after 48 hours d had maximum titre (about 10^4 LD50) 72–96 hours r infection falling to a low level at 168 hours; virus s first detected in the brain after 72 hours after which titre rose steadily up to the 9th day. These results gest that virus enters the bloodstream primarily ough the lymphatic system and that multiplication may ur in the lymph nodes. *C. E. Gordon Smith*

RDOS, V. **Immunological Study of Antibodies neutralizing Tahyna Virus in the Sera of Inhabitants of Czechoslovakia.** *J. Hyg., Epidemiol., Microbiol. & Immunol.* Prague. 1960, v. 4, No. 1, 54–60, 1 fig. [16 refs.]

Strain 92 of Tahyna virus [this *Bulletin*, 1960, v. 35, 7] after 4–14 mouse passages was used. Neutralization ts were carried out with undiluted inactivated sera xed with dilutions of virus, incubated for 2 hours at °C. then inoculated intracerebrally into mice. Prelimin-y tests were made with mixtures of sera then individual a against 50–100 LD50 of virus. The sera were from ployees in the food industry or patients in antenatal nics. In 2 low-lying marshy regions with very high nual populations of *Aëdes vexans*, one in south-east d one in south-west Czechoslovakia, the incidence of antibody was 30%. In neighbouring less marshy regions with irregular mosquito populations the incidence was only 13%. Elsewhere in Czechoslovakia where mosquito populations are low, the incidence was 2%. The neutralizing indices ranged from 100 to 6,920.

C. E. Gordon Smith

DROZDOV, S. G. **Experimental Study on the possibility of Isolation of 4 Virus Strains belonging to the Tick-Borne Encephalitis Group from Goat's Milk.** *J. Microbiol., Epidemiol. & Immunobiol.* London. 1959, v. 30, No. 3, 144–9, 1 fig. [Translated from Russian.]

10 goats aged 2 or more years whose milk and blood was uninfected with agents pathogenic for mice and which were without antibody to the viruses studied, were infected in pairs with the following viruses: tick-borne encephalitis (Strain No. 4), louping ill, Omsk haemorrhagic fever (Strain GOL), biphasic milk fever (Strain F of human origin and Strain K-57 from goats' milk). 2 doses of 5 ml. of 10% mouse-brain suspension were given 1–2 days apart, subcutaneously or intramuscularly. From the 3rd day blood and milk samples were tested every 1–2 days. The GOL, No. 4 and K-57 strains caused no detectable signs of illness in the goats. Strain F caused langour, anorexia and some fever. Louping ill in 1 animal caused disorders of co-ordination, tremors and loss of skin sensation 6 days after infection. Weakness of limbs, periodic opisthotonus and tachypnoea followed; on the 8th day the animal had convulsions and died. At post mortem virus was isolated from the brain and also from the brain of a foetus *in utero*. In the other animal there was only transient weakness and anorexia.

Virus was isolated at 1st passage from the blood of at least 1 animal infected with each virus [? except K-57] 3–6 days after infection and from the milk of at least 1 animal infected with each virus 6–8 days after infection. The doses given were, however, larger than are likely in nature. All the animals had developed complement-fixing antibody 20–40 days after infection.

C. E. Gordon Smith

DROZDOV, S. G. **The Nature of Biphasic Milk Fever (from Data obtained in Studies of a Focus in the European Part of the U.S.S.R.). I. Isolation of Strains of the Virus and their Characteristics.** *Problems of Virology.* London. 1959, v. 4, No. 2, 77–81. [Translated from Russian.]

The literature on the differences between tick-borne Russian spring-summer encephalitis and milk-borne biphasic meningo-encephalitis is discussed. In the spring of 1953 a study was made of biphasic milk fever in 6 villages in Moscow Oblast. By intracerebral inoculation of mice the strain F was isolated from the blood of a patient in the 3rd day of illness, 4 strains (K-54, K-57, K-12, K-15) were isolated from goats' milk, and the strain *Ixodes ricinus* 99 was isolated from ticks. One blind passage was used where necessary [but it is not stated in which strains]. All the strains were filterable. All could be preserved in mouse-brain in 50% of glycerol at 2–4°C. for at least 5 months, freeze-dried for at least

1½ years. Virus in frozen [? −5 to −10°C.] brain suspension [?10% brain in Ringer's solution with the 50% inactivated guineapig serum] was preserved for at least 6 months and in frozen whole brain for at least 9 months. In suspensions virus remained viable for at least 2½ months, at 2–4°C. for 20–30 days at 20°C., up to 3 days at 37°C. Boiling destroyed virus in 2–3 minutes. The virus resisted ethyl alcohol and diethyl ether for 3 days [conditions not specified]. A dilution of 1:500 formalin inactivated virus within 14 days at 2–4°C. without destruction of immunogenicity.

The viruses had approximately the same infectivity titre in mice by all inoculation routes. Guineapigs and cotton-rats were insusceptible. Strain F given intracerebrally to a kid caused severe encephalitis and paralysis but peripheral inoculation of young and adult goats and cows caused no symptoms. Viraemia however resulted in both goats and cows and in lactating animals virus appeared in the milk. Chick embryos were infected and after passage died in 2–4 days. In mice infected with strain F the log titres in various organs were: brain 7·5, liver 4·2, spleen 4·0, kidney 3·7, lung 3·2, blood 2·5.

C. E. Gordon Smith

ŠIMKOVÁ, A. **A Study on the Prophylactic Application of Immune Gamma-Globulin in Tick-Borne Encephalitis.** *Acta Virologica.* Prague. 1959, Oct., v. 3, No. 4, 240–49, 6 figs. [15 refs.]

The strain "O" of Russian spring-summer virus after 27 or more mouse passages were used. A ram was immunized with 5 inoculations of mouse-brain suspension purified with bentonite together with adjuvants. γ-globulin was prepared by alcohol fractionation from the sheep serum and from the sera of human convalescents. Groups of mice were given doses of 0·05–1·0 gm. of 2% γ-globulin per kgm. body weight intramuscularly. Their sera were tested at intervals in a subcutaneous neutralization test in suckling mice: mice receiving 1 gm./kgm. had neutralizing indices of 80 after 24 hours, 120 after 3 days, 400 after 7 days, 640 after 10 days and 120 after 20 days; mice receiving 0·05 gm./kgm. had neutralizing antibody at a low level for about a week; and the other doses gave immediate levels and durations. At various dose levels mice were challenged with 5 or 50 subcutaneous LD50 of virus at various intervals: 96% of the animals challenged up to 7 days after γ-globulin survived, and 86% after 14 days down to a dose of 0·01gm./kgm. of γ-globulin. After 30 days 55% of mice were protected.

The persistence of antibody in non-immune human volunteers after administration of normal human γ-globulin was studied: after 0·3gm./kgm. of 10% γ-globulin average neutralizing indices of 80, 120, 130 and 70 were found after 1, 3, 7 and 14 days respectively—after 4 weeks no antibody was detected. Antibody studies were also made of similar volunteers given 2% γ-globulin from human convalescents. The average log neutralizing indices were 2·7, 3·3, 3·3, 3·1, 2·8, 2·3, 2·2, 1·5 after 1, 3, 7, 14, 21, 28 days, 6 weeks and 8 weeks respectively. The recommended minimum antibody titre for such γ-globulins is that 50 LD50 of virus should be neutralized by a 1:150 dilution.

C. E. Gordon Smith

HAMMON, W. McD., RUDNICK, A. & SATHER, G. **Viruses associated with Epidemic Hemorrh Fevers of the Philippines and Thailand.** *Sci* 1960, Apr. 15, v. 131, 1102–3.

A number of children suffered a serious, frequ fatal, haemorrhagic febrile illness in Manila in the season in 1954 and this was named Philippine haem hagic fever. A large epidemic occurred during the season in Manila in 1956. 750 cases occurred bet July and October with approximately 10% deaths. predominant age-group was below 6 years. It occurr areas with plentiful *Aëdes aegypti* but not in the pres of *Aëdes albopictus* without *Aëdes aegypti*.

In Bangkok a haemorrhagic disease was first recog in 1954 and a large epidemic occurred in the rainy se of 1958 with about 2,500 patients admitted to ho and 250 deaths. There were some clinical differ from the Manila outbreak but the seasonal and d distributions were similar as was association with *aegypti*. Mosquitoes and acute phase sera were to Pittsburgh and inoculated into suckling mice. Su ing mice were challenged with dengue-2 virus immunity frequently found.

From Manila 14 viruses were isolated in suckling —adaptation required 10–20 passages. Except f strain which was dengue-2, they were of 2 new of dengue (3 and 4) which were antigenically relat types 1 and 2. 9 type 3, 2 type 4 and 1 type 2 vi were isolated from human sera. Type 3 was isolated from *Aëdes aegypti* and once from *Culex tritaenio chus.*

From Bangkok 3 strains of type 2 virus were isc from *Aëdes aegypti*, 3 of type 2 from human sera a of chikungunya (Group A) also from human ser strains of chikungunya and 1 (probable) type 1 were isolated by other workers. 1 further agent isc appears to differ from the above.

Studies of paired sera have shown rises in antibo the Group B, and Group A agents and, in some pa to both simultaneously. Some patients showed no body response to either. [The authors suggest ar-bo- instead of arborvirus as the abbreviation for arthro borne zoonoses virus]. *C. E. Gordon Sm*

HALLAUER, C. Züchtung von Gelbfiebervirus in m chlichen Explantaten. **[The Cultivation of Ye Fever Virus in Human Tissue Cultures]** *f.d. gesamte Virusforschung.* 1959, v. 9, No. 3, 41. [16 refs.]

[An abstract of this paper appeared in the *Tro Diseases Bulletin*, 1960, v. 57, 803.]

BECH, V. **Studies on the Rate of Multiplicatio Measles Virus in Rhesus Monkey Kidney Cultures.** *Acta Path. et Microb. Scandin* 1958, v. 44, No. 3, 299–306.

A study has been made of the rate of multiplic in rhesus monkey kidney cell cultures of the I a strains of measles virus, which had been isolat

enhagen. Syncytia were observed after 48 hours, and cells became detached from the glass after 3–4 days. nplement-fixing antigen appeared after the second Infective virus appeared after about the same time.
D. J. Bauer

KAWA, S., MUTO, S., KANEKO, T. & SEKI, T. **Experimental Studies on Canine Distemper Virus (CDV). Report 1. Experiment on the Isolation of the Virus in Mice and Embryonated Eggs and the Relation of the Mouse-Adapted CDV to Mouse-Fixed Measles Virus and Others.** *Yokohama Med. Bull.* 1959, Aug., v. 10, No. 4, 179–89. [38 refs.]

he Ebisu, Tomonaga and Minami strains of canine mper virus isolated from the sera of infected dogs n during the febrile period could be adapted to intracbral passage in 6–7 gm. mice after several passages he chorioallantoic membrane. The strains were shown e identical wih a reference strain (J) of canine disper virus in cross-neutralization tests. A rise in titre eutralizing antibody to the J strain was observed in g infected with distemper. The strains of distemper s were also neutralized by measles antisera to high s, but did not react with antisera to 9 other viruses ntained in the same laboratory, including ectromelia.
D. J. Bauer

TUMOTO, M., MUTAI, M., AOYAMA, Y. & OIKAWA, T. Virus HSO, virus cytopathogénique, isolé sur la culture des cellules HeLa à partir du sérum de sujet humain sain. [**A Cytopathogenic Virus HSO (Human Serum Orphan) isolated in HeLa Culture from the Serum of a Healthy Human Subject**] *C.R. Soc. Biol.* 1959, v. 153, No. 10, 1660–63, 1 fig. [16 refs.]

The following is a translation of the author's summary:—

A cytopathogenic virus was isolated from the serum of a healthy human subject, and its properties were studied. It seems to differ from other viruses, and for the moment is referred to as HSO (Human Serum Orphan). Neutralizing antibodies have been found in a high proportion of the people [in Tokyo and Ibaraki]. It is not known if the virus causes disease.
Charles Wilcocks

LAVILLAUREIX, J. & REEB, E. Note préliminaire sur un virus isolé au cours d'affections pneumoniques épidémiques. [**Preliminary Studies on a Virus Isolated from Cases of Epidemic Pneumonia Infections**] *Ann. Inst. Pasteur.* 1960, May, v. 98, No. 5, 754–7, 4 figs. on 2 pls. [12 refs.]

The English summary appended to the paper is as follows:—

"The size of the virus is 30 to 50mμ. It is resistant to ether, and haemagglutinating. In tissue cultures, it induces a proliferation, followed by a secondary necrosis. It was not possible to identify this agent with any known virus."

BURNET, F. M. & STANLEY, W. M. **The Viruses. Biochemical, Biological and Biophysical Properties. Vol. 2. Plant and Bacterial Viruses. Vol. 3. Animal Viruses.**

These books were reviewed on pp. 526 and 527.

IMMUNITY

BOS, R. J. & SCHAEDLER, R. W. **The Effect of the Intestinal Flora on the Growth Rate of Mice, and on their Susceptibility to Experimental Infections.** *J. Exper. Med.* 1960, Mar. 1, v. 111, No. 3, 407–17.

Establishment of a colony of "disease-free," or pecific pathogen-free," laboratory animals is an interng and thought-provoking experiment: readers should nsult the original paper for a stimulating discussion on possible implications of such work, and suggestions the study of nutritional, bacteriological and immunoical problems.

From 3 pregnant Swiss albino mice, 12 surviving young males and 5 females) delivered by Caesarian section, re maintained in an environment protected from con- t with common mouse pathogens, but not in a comtely germ-free state. Details of the colony will be preited elsewhere by Dr. John NELSON and Mr. George LLINS who established it in the Rockefeller Institute.

This paper summarizes the results of comparative studies on almost 4,000 animals in the so-called NCS (Nelson-Collins-Swiss) colony and a similar number in the SS (standard Swiss) colony.

The NCS mice not only grew more rapidly than the SS mice on complete diets, but even continued to gain weight (at a slower rate) on diets so deficient that SS mice stopped growing and lost weight. They proved more susceptible than SS mice to certain experimental bacterial infections, but, in contrast, were more resistant to the lethal effect of large doses of endotoxins. (Injection, however, of minute amounts of these endotoxins caused a marked increase in susceptibility to staphylococcal infections.)

These striking peculiarities of the NCS mice could be rapidly obliterated by contaminating them with a culture of *E. coli* derived from the SS mice: it was consistently found that the intestinal flora of the NCS mice differed qualitatively from that of the SS group, lacking in particular the Gram-negative lactose fermenters (*E. coli*) found invariably in the latter.

This experimental mouse colony raises new problems and queries about not only nutritional requirements of animals but also the factors which condition resistance to bacterial diseases. For example, the NCS mice were found to develop a marked increase in resistance to tuberculosis following vaccination with living BCG or with killed mycobacterial antigens, and their resistance to a variety of bacterial infections could be increased in a non-specific manner by prior treatment with unrelated endotoxins. *D. A. Cannon*

NOSSAL, G. J. V. **Antibody Production by Single Cells. IV. Further Studies on Multiply Immunized Animals.** *Brit. J. Exper. Path.* 1960, Feb., v. 41, No. 1, 89–96, 2 figs. [11 refs.]

This paper presents further results of an investigation which has already been reported in part [this *Bulletin*, 1959, v. 34, 403, 958; 1960, v. 35, 322]. Rats were injected in the footpad with 2 or more of the serologically unrelated flagellar antigens of Salmonella Adelaide, 2 transductional derivatives of *Salmonella paratyphi* B, and a transductional derivative of *Salmonella typhi*. Single plasma cells from the local lymph nodes were introduced into microdroplets of medium which were incubated at 37°C. to allow antibody to pass from the cell into the medium. Antibody in droplets was determined by the immobilization of motile homologous salmonellae introduced into the droplets. When one type of salmonella had been introduced to test for homologous antibodies, the organisms were completely immobilized by a known excess of their own antiserum before another type of salmonella was introduced to test for another antibody.

In 17 experiments the same 2 antigens were injected together in various concentrations, each rat receiving 2 doses 4–6 weeks apart. Of 519 cells examined, 103 produced antibody to one of the antigens and 22 formed antibody to the other. Different pairs of antigens gave similar results in 6 further experiments. In 10 experiments 3 antigens were injected together. Of 351 cells tested for the 3 types of antibody, 50 produced one type, 29 the second type, and 25 the third. Two antigens, in oil and water emulsions to give an adjuvant effect, were given separately at an interval of 7 weeks. Of 165 cells tested, 9 produced one antibody and 21 the other. In 5 experiments 2 injections of one antigen were given at a 4-week interval, 1 injection of a second antigen 2 days after the second of the 2, and finally 4–6 weeks later 1 injection of a mixture of both. Of 154 cells tested, 27 produced one antibody and 8 the other.

In none of these experiments did any one cell produce antibody to more than one antigen. *I .B. R. Duncan*

BECKER, E. L. **Concerning the Mechanism of Complement Action. V. The Early Steps in Immune Hemolysis.** *J. Immunology.* 1960, Mar., v. 84, No. 3, 299–308, 3 figs. [19 refs.]

This is another paper from the Division of Immunology, Walter Reed Army Institute of Research, on the interaction of the different components of complement in the early stages of immune haemolysis. [See this *Bulletin*, 1959, v. 34, 589.]

It is now possible to obtain the complement frac C'1, C'2 and C'4 free of each other and therefo study the order in which the fractions function an role that each plays, and the author summarizes his ings as follows:

"In confirmation of previous work it has been f that C'1 can bind to the sensitized red cell in an he tically active form in the absence of the other co nents. The attachment of C'1 and its subsequent rem leaves a sensitized cell which does not differ from a which never had been in contact with C'1 in its sus bility to hemolysis by whole complement or in its a to again bind C'1.

"The attachment of C'1 is necessary for the bi of C'4 activity, however; C'1 can then be removed the cell will still retain C'4 activity. The presence of C'1 and C'4 activity is required for the uptake o activity. However, once C'2 activity is attached C'1 longer required; its function has been performed. C' be removed and the cell will still be able to lyse i presence of C'3 as long as C'2 activity remains on cell.

"These facts lead to the view that with regar immune hemolysis C'1 does nothing more to the sens cell than attach itself. Once on the cell C'1 acts C'4 and C'2 preparing and allowing their activities to to the sensitized cell. C'1 on the cell inactivate diisopropylfluorophosphonate (DFP) is no longer ca of binding C'4 or C'2. This leads to the inference it is the enzymatic action of C'1 on C'4 and C'2 w leads to their being bound. C'1 does not play a ro the decay of C'2 on the cell." *D. A. Cann*

JENKINS, G. C., POLLEY, Margaret J. & MOLLISON, P **Role of C'_4 in the Antiglobulin Reaction.** [C spondence.] *Nature.* 1960, May 7, v. 186, 4 1 fig. [15 refs.]

HOOK, E. W. & WAGNER, R. R. **The Resista Promoting Activity of Endotoxins and C Microbial Products. I. Their Effect on *Sa nella typhosa* Infections of Mice.** *J. Immuno* 1959, Sept., v. 83, No. 3, 302–9, 3 figs. [27 **II. Protection against the Neurotoxic Actio Influenza Virus.** *Ibid.*, 310–17, 2 figs. [37 re

I. Experiments showed that the increased non-sp resistance to *Salmonella typhi* infection which follow injection of *Escherichia coli* endotoxin depends o route of injection of the protective and challenge inc For instance mice receiving 10 μgm. of endotoxin peritoneally were much more resistant to a perit injection of *Salm. typhi* than animals into whic same amount of endotoxin was injected subcutane intravenously, or intracerebrally.

With cerebral typhoid infection the importance o route of the protective injection of endotoxin was more striking. Endotoxin introduced intraperitoneal intravenously was followd by a 4-fold rise in resistan calculated by LD50, but the resistance was 300 greater than in controls when the endotoxin was inj intracerebrally.

he rate of multiplication of *Salm. typhi* in the brains mice infected intracerebrally with 3×10^5 organisms followed by means of viable counts. Controls and e which had received endotoxin intracerebrally were ed at intervals. 4 hours after infection both groups e similar counts but after 24 hours the bacteria in controls ranged from 10^6 to 10^8 whereas in the pre-ted animals the average was about 10^3.

he typhoid bacilli persisted in the brains of pre-treated e for more than 10 days but did not reach the nbers found in the controls which died on the 3rd day. ppears that the protective effect is exerted by prevent- the concentration of typhoid bacilli from reaching a al concentration without eradicating the infection.

ncreased resistance to cerebral typhoid was obtained effectively with intracerebral injection of heat-killed phoid bacilli as with 10 μgm. endotoxin. Xerosin, an l precipitable fraction from *Achromobacter xerosis*, ough not so striking in its effect increased resistance 7 times. It is thought that the protective effect of osin and typhoid vaccine is attributable to their endo- in content.

Mice injected intracerebrally with sublethal amounts of uenza virus or a concentrated suspension of a non-ectious heat-treated virus, were found to have a slightly reased resistance to cerebral typhoid.

I. This work describes an extension of that described the previous paper. It was found that purified endo- in from Gram-negative organisms or heat-killed phoid bacilli injected intracerebrally greatly diminished neurotoxic effect on mice caused by the injection of ssive doses of a non-neurotropic influenza virus.

The protection was similar to that achieved by endo- in against cerebral infection by typhoid bacilli. It s most pronounced when the endotoxin was injected racerebrally and the onset of resistance to the toxic ect of the virus gradually increased in 1–3 hours after protective injection being maximal in 6–24 hours. e toxic effect was measured by convulsions and subse-ent death of the animals. In protected animals there s no evidence that multiplication of the virus had curred *in vivo*.

Endotoxin failed to protect mice against infection used by injecting either the adapted NWS neurotropic us or the virus of lymphocytic-choriomeningitis.

Douglas D. Smith

EEDMAN, H. H. **Passive Transfer of Protection against Lethality of Homologous and Heterologous Endotoxins.** *Proc. Soc. Exper. Biol. & Med.* 1959, Nov., v. 102, No. 2, 504–6.

The serum of rabbits rendered tolerant to endotoxin from *lmonella typhi* was found to protect mice against the hal effect of the same endotoxin or one derived from a ain of *Escherichia coli*. The protection did not depend the antibody content of the serum as the maximum re achieved against the homologous endotoxin was only 16 and no antibody was demonstrated against the *E. li* endotoxin.

Rabbits were rendered tolerant by the daily injection endotoxin, in doses rising from 2·5 to 10 μgm. for 6 ys. The serum was taken from animals when they were killed 20 hours after the last injection. Serum from endotoxin-protected animals protected mice against the homologous and the heterologous endotoxin administered intraperitoneally. Protection occurred whether the serum was injected intraperitoneally or intravenously. It was not possible to say whether the degree of protection against each endotoxin was exactly the same.

Douglas D. Smith

OVARY, Z. & KARUSH, F. **Studies on the Immunologic Mechanism of Anaphylaxis. I. Antibody-Hapten Interactions Studied by Passive Cutaneous Anaphylaxis in the Guinea Pig.** *J. Immunology.* 1960, Apr., v. 84, No. 4, 409–15. [18 refs.]

FRUHMAN, G. J. **Mobilization of Neutrophils into Peritoneal Fluid following Intraperitoneal Injection of Bacterial Endotoxins.** *Proc. Soc. Exper. Biol. & Med.* 1959, Nov., v. 102, No. 2, 423–5. [12 refs.]

Contrary to frequent reports the author has found that the injection of 0·9% NaCl into the peritoneum of rats does not provoke the flow of neutrophils into the peritoneal cavity. The reason for his finding he attributes to the fact that he used pyrogen-free sterile saline. A marked local neutrophilia was produced when certain bacterial products were added to 10 ml. saline and injected intraperitoneally. The bacterial extracts used were Piromen, a *Pseudomonas* polysaccharide complex, staphylococcus A lipopolysaccharide, and a lipopolysaccharide from a strain of *Escherichia coli*. It was found that to produce a neutrophil response required the addition of as little as 0·0001 μgm. of the staphylococcal product and 0·001 μgm. of the other 2 extracts.

It is suggested that for a detection of pyrogenic bacterial derivatives the method described in this paper would be more satisfactory than that based on the febrile response of rabbits. *Douglas D. Smith*

ROWLEY, D. & WHITBY, J. L. **The Bactericidal Activity of Mouse Macrophages** *in vitro*. *Brit. J. Exper. Path.* 1959, Oct., v. 40, No. 5, 507–15, 3 figs. [10 refs.]

Macrophages from mouse peritoneum were infected *in vitro* in order that the fate of phagocytosed bacteria might be studied. The peritoneum of a freshly killed mouse was washed out with 1·5 ml. of a tissue-culture medium containing heparin. One ml. of this peritoneal eluate was added to Porter flasks of 3·5 cm. internal diameter on the bottom of which had been placed a "flying coverslip." After 3 hours' incubation at 37°C. the heparinized medium was removed and replaced by 1 ml. of fresh medium containing bacteria. At intervals flasks were removed and bacterial counts were made by plating out aliquots of the supernatant in order to determine the numbers of unphagocytosed bacteria; simultaneously the "flying coverslip" with macrophages was removed, inverted on MacConkey's medium and spread around vigorously to aid in the disruption of the cells.

Bacteria from overnight cultures were treated with a heat-treated specific agglutinating rabbit antiserum. When these pretreated organisms were added to the flasks containing the macrophages they disappeared from the supernatant so that 70 minutes after infection, 77% had been phagocytosed and of these only 31% were viable. On the other hand organisms pretreated with normal rabbit serum multiplied in the supernatant and the bacterial counts rose steadily from the time that they were added to the macrophage cultures.

Organisms used for these experiments included 3 strains of *Bacterium coli,* 1 strain of *Bact. friedlanderi* and 2 strains of *Salmonella typhi-murium,* one of which was highly virulent and the other not. It was found that the macrophages were in all cases capable of killing each of these organisms when opsonized and that the rate of killing was of a similar order for all of them.

Macrophages obtained from mice specifically immunized against a strain of *Bact. coli* were no more effective in destroying the opsonized homologous organism than were normal macrophages.

A modification of the experimental procedure was adopted in which 30 minutes after infection of the macrophage cultures the supernatant containing unphagocytosed bacteria was removed and replaced with fresh medium. The object of this manoeuvre was that the bactericidal rate might be studied free from the interference of continued phagocytosis and extra cellular multiplication.

By this method it was found that the rate of killing by the macrophages agreed with the results obtained from the experiments in which the bacteria were not removed from the supernatant. [See also this *Bulletin,* 1960, v. 35, 324.] *Douglas D. Smith*

HIRSCH, J. G. & CHURCH, Alice B. **Studies of Phagocytosis of Group A Streptococci by Polymorphonuclear Leucoytes** *in vitro. J. Exper. Med.* 1960, Mar. 1, v. 111, No. 3, 309–22, 5 figs. [12 refs.]

It has been long known that there is a difference between human blood and rabbit blood in their capacity to phagocytose and kill Group A streptococci *in vitro.* It is apparent also that some streptococci possess 2 surface components, M protein and hyaluronic acid, either or both of which are able to protect bacteria from engulfment by leucocytes under certain conditions.

The authors first studied the fate of Group A streptococci (from young and old cultures) when added to rabbit peritoneal exudates containing 25,000 granulocytes per cmm. (over 95% polymorphonuclears), and the effects of hyaluronidase and of antiserum on the susceptibility of various strains of streptococci to phagocytosis by suspensions of rabbit granulocytes. They showed that encapsulated streptococci resisted phagocytosis in rabbit leucocyte-rabbit serum system, and went o study the phenomenon using human leucocytes (prep from blood by the dextran sedimentation technique) pended in Gey's solution.

They found that the addition of antibody to M pr to such phagocytic test systems, using rabbit serum, not render the streptococci susceptible to phagocy since the hyaluronic acid capsule of the organism tinued to interfere with phagocytosis. But human se was found to contain a factor which counteracted the phagocytic effect of the streptococcal hyaluronic capsule, and so human blood could be used to d antibodies which combine with the only other ph cytosis-resisting component of the organism, namely M protein. The nature of this factor is unknown appeared to be neither an antibody nor an enz capable of depolymerizing hyaluronic acid. But it a possible explanation for the suitability of human compared with rabbit, blood for opsonophagocytic to measure type-specific streptococcal antibodies.

D. A. Cann

HIRSCH, J. G. **Further Studies on Preparation Properties of Phagocytin.** *J. Exper. Med.* Mar. 1, v. 111, No. 3, 323–37.

Continuing his studies of phagocytin [this *Bulletin,* v. 31, 1051, 1143] the author describes experimen show that phagocytin and histone B [*Ibid.,* 1959, v 476] are separate entities for the following reasons peptic digestion destroys the bactericidal action of his but not that of phagocytin; (b) spermine antagonize lethal effect of phagocytin on coliform bacteria much than it does that of histone; (c) phagocytin may b tracted from disrupted granulocytes with dilute acid, but the extraction of histone requires a stro mineral acid or salt solution; (d) phagocytin is lim in distribution to polymorphonuclear leucocytes, v histone is demonstrable in monocytes, thymus, liver, ney, lung, etc.

Phagocytin, obtained free of lysozyme and histone fractional extraction based on the Mirsky-Pollister nique, was capable of killing Group A streptococci staphylococci as well as Gram-negative bacilli. C acid extracts of granulocytes from man, rabbit, horse guineapig (the only species so far tested) all conta phagocytin; circulating leucocytes as well as exudate contained it.

The chemical nature of phagocytin is not yet clea appears that the active ingredient is non-dialysable can be precipitated by trichloracetic acid.

D. A. Cann

Miscellaneous

RLD HEALTH ORGANIZATION. TECHNICAL REPORT SER. NO. 187. **Expert Committee on Biological Standardization. Thirteenth Report. Geneva, 31 August–5 September 1959.** 49 pp. [Refs. in footnotes.] 1960. Geneva: Palais des Nations. [Sales agent for U.K., H.M. Stationery Office.] [3s. 6d.; $0.60; Sw.fr. 2.–.]

his report is divided into several main sections:— (1) rmacological, which has paragraphs on standardiza- of 14 antibiotics; (2) Immunological, which deals antigens, antibodies and veterinary standards; (3) logical Diagnostic Reagents; (4) Requirements for Biological Substances. There is an annex which contains a long table (20 pages) of international biological standards and international biological reference preparations, a short table of proposed standards and preparations, and a list of discontinued standards.

Charles Wilcocks

LABORATORY ANIMALS CENTRE. **Report of a Symposium on Quality in Laboratory Animals held at the Royal Veterinary College, London, on 16th April, 1959.** *L.A.C. Collected Papers.* 1959, v. 8, 68 pp., illustrated. [Numerous refs.]

Book Reviews

ITH, George [M.Sc., F.R.I.C., M.I.Biol.] **An Introduction to Industrial Mycology.** Foreword by Harold RAISTRICK, Sc.D., F.R.S., 5th Edition pp. xvi + 399, 168 figs. 1960. London: Edward Arnold (Publishers) Ltd., 41, Maddox Street, W. 1. [40s.]

The latest edition of this useful book closely resembles immediate predecessor [this *Bulletin*, 1954, v. 29, 23] from which it differs in a modest increase in size, a few additional illustrations, in many small alterations d additions necessitated by recent, especially taxono- c, work on fungi, in a green cover instead of the niliar blue one, and in a 33⅓% increase in price.

Readers of this *Bulletin* should not be deterred by the e. This book provides an outstanding, and still not duly expensive, introduction to the practice of culture, examining, and identifying common moulds for any- e having an interest in mycotic infections of man or imals, fungus-spore allergies, antibiotics produced by ngi, or the fungal contaminants of bacterial cultures. here is also much information on general mycological ocedures not always easily found elsewhere and the ok can be warmly recommended as a supplement to xts on more clinical or applied aspects of mycology.

G. C. Ainsworth

ILKINSON, P. B. [M.R.C.P.] **Variations on a Theme by Sydenham—Small-Pox.** 40 pp., frontispiece & 40 figs. on 35 pls. 1959. Bristol: John Wright & Sons Ltd.

Though this book was published in 1959 it was written the 1930's, its contents being based on the experience of its author during the epidemic of smallpox in Hong Kong in 1937-38. It is, therefore, a monograph, not on smallpox as a whole, but on one particular epidemic of variola major in a (mainly) coloured population which took place before recent advances in virology, in antibiotic and other forms of therapy, and modern views on the pathogenesis of the pock diseases had become established. Thus, to the author, modified smallpox means only "smallpox occurring in people who have at some time in their lives been vaccinated," and "serologically we know nothing about smallpox." But the clinical features of smallpox do not change and the descriptions of certain forms of the disease to be found in this book are as fine as any in the literature of the subject. Especially, perhaps, is this true of the section on toxic smallpox. The influence of RICKETTS upon the author is plain, and at times the phraseology of the two is almost identical, but the author introduces a number of descriptive terms which to the reviewer are both new and attractive. For example, "honeycomb stage" for the beginning of involution, "the appearance of the first beads of pus exuding from their pustules is exactly like that of honey exuding from a comb": "mother-pock" (for "protopapule"); "macaroon facies," "her face looked exactly like the bottom of a macaroon with the rice paper flaking off it": and "horn pox" for the granulomatous termination of the modified lesion on the face.

The 68 photographic illustrations, so important a part of any description of smallpox, adequately support the text. In the legend under Fig. 30 the words "centrifugal" and "centripetal" should be transposed.

The book is attractively produced, though some readers, like the reviewer, may find the type a little too small for their comfort. It is a very worthy addition to an exclusive list of monographs on smallpox written by clinicians from their own experience.

J. Pickford Marsden

BURNET, F. M. **Principles of Animal Virology.** 2nd Edition. pp. ix + 490, frontispiece & 34 figs. 1960. New York 3: Academic Press Inc., 111, Fifth Avenue, N. Y. London: 17 Old Queen Street S.W.1. [$12.00]

This is the best text-book for the student of animal virology because it deals with the principles in an orderly and exceptionally readable manner and yet is packed with illustrations from the literature which are discussed with considerable insight. Such is the pace of development in virology that a new edition has become necessary within 5 years [see also this *Bulletin*, 1956, v. 31, 765]; nearly half the text has been re-written but, remarkably, without any increase in length—a formidable achievement when nearly every text book expands with each edition.

The main sections re-written are, of course, those fields in which there have been the most important changes in the past 5 years; the physical and chemical structure of viruses, multiplication and liberation of virus from host cells and the morphological and functional changes observable in the latter, interference, and the pathogenesis of virus diseases.

The section on immunity embraces the author's clonal selection theory of antibody formation, and the sections on ecology, variation, evolution and classification are brought up to date. *C. E. Gordon Smith*

FLOREY, M. E. [M.D.] **The Clinical Application of Antibiotics. Vol. IV. Erythromycin and other Antibiotics.** pp. viii + 303, illustrated. 1960. New York. Toronto. London: Oxford University Press, Amen House, Warwick Square, E.C.4. [84s.]

This volume deals in considerable detail with many newer and lesser-known antibiotics as well as with some that are older but whose place in therapeutics has taken some time to establish. In the first 6 chapters each drug is dealt with separately; antibacterial activity, administration, absorption, distribution in tissues and toxic effects are assessed with constant reference to reports of clinical and laboratory trials. An attempt is made at the end of most sections to reach some conclusion about the drug's place in therapeutics. Some idea of the scope of the book may be given by mentioning some of the antibiotics dealt with:—erythromycin, carbomycin, oleandomycin, vancomycin, ristocetin, amphomycin, neomycin, polymixin, tyrothricin, gramicidin, nystatin, framycetin and many more. The last chapter deals with the choice of antibiotic in specific conditions and relates not only to the drugs mentioned in the book but to others already dealt with in previous volumes, namely penicillin, streptomycin, chloramphenicol and the tetracyclines. This chapter can be read with great profit on its own, the rest of the volume being used as a reference book for information not easily obtained elsewhere. The book is thoroughly recommended for inclusion in hospital and laboratory libraries. *A. B. Christ*

WAKSMAN, Selman A. **The Actinomycetes. Vol Nature, Occurrence and Activities.** pp. xi + frontispiece & 107 figs. 1959. London: Baill Tindall & Cox, Ltd., 7 & 8, Henrietta Street, W. [£5.]

The present volume is the first of a series of th designed to cover all present-day knowledge concer the Actinomycetes and their activities. The book g a general picture of what the Actinomycetes are, how are isolated and studied, distribution in nature, phy logy and biochemistry, and economic importance, p cularly in agriculture and medicine. Taxonomy is t treated fully in Volume II, so only the broad princi of classification are considered here.

The author has, for more than 40 years, made class of organisms his special study, and has alr published a long series of papers and books on subject. In the epilogue to this volume he states "I presented in these pages my personal experiences with actinomycetes." If this were literally true the book w be both more interesting and more digestible. As i it gives the impression of a vast card-index, which been expanded to make it readable, but all of which perforce to be included. It is far too much in the na of a catalogue of all the investigations which have carried out on these organisms. Completely contradic statements are put down side by side without comm from the author. Also there is overmuch repeti giving the impression that each chapter had been wr without reference to the rest. For example, antibiotic discussed in some detail in Chapter 9, on biochemi Chapter 15 is devoted entirely to the subject, and Vol III in this series is to be concerned exclusively with biotic production.

There are numerous illustrations, many of which excellent. Unfortunately, a number of the pictures far removed from the relevant text, and some of t are not referred to at all.

There is a long and valuable bibliography at the of the book. It is, however, a pity that the names of journals are not in standard form, and are not italici

The misprints noted are very few and mostly u portant, and the production is of a high standard.

It is a tantalizing book, but, in spite of its faults, it be of great value to all who are studying this interes but puzzling group of organisms, since it covers the ject adequately from all angles, and contains a amount of information. *G. Smi*

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